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ACUTE CONTAGIOUS DISEASES.

BY

WILLIAM M. WELCH, M.D.,

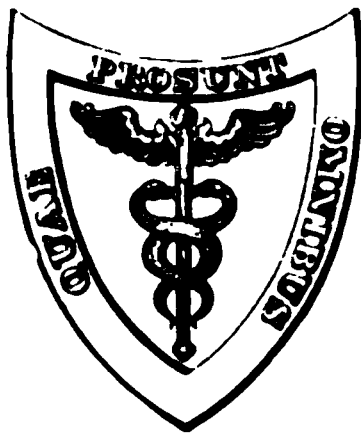
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ILLUSTRATED WITH 109 ENGRAVINGS AND 61 FULL-PAGE PLATES.



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PREFACE.

IN this work on Acute Contagious Diseases the writers have endeavored to present a practical treatise for the guidance of students and practitioners of medicine.

Perhaps some explanation may be sought for the adoption of the title. We have somewhat arbitrarily included in this work but a small group of diseases, particularly those with which we have had experience in the Municipal Hospital of Philadelphia. The use of the term "infectious diseases" would have necessitated the inclusion of a great number of maladies upon which we do not feel specially qualified to write. Furthermore, the group of contagious diseases is distinguished by great transmissibility, being communicated by the merest contact or even by proximity, and therefore the term in its strict etymological sense appears to us to be justified. Vaccinia is, of course, not contagious, but its relation to the prophylaxis of smallpox makes the consideration of the two inseparable.

The comparative infrequency of epidemics of smallpox renders it quite possible for accomplished and otherwise experienced physicians to be somewhat unfamiliar with this disease. We have, therefore, devoted to this affection, and particularly to its diagnosis, an amount of space not usually accorded to it in text-books of medicine.

We have furthermore endeavored to elucidate the subject-matter with numerous photographs of patients under our care. The text is based upon a personal study of over 9000 cases of smallpox, 9000 cases of scarlet fever, and 10,000 cases of diphtheria, in addition to a considerable number of cases of the other diseases discussed, all of which have been treated in the Municipal Hospital of Philadelphia during the past thirty-five years.

We desire to acknowledge our indebtedness to Dr. E. L. Graf, formerly Resident Physician in the Municipal Hospital, for assistance in securing some of the photographs; to Dr. Burton K. Chance, for the contribution of the chapters on Eye Complications and Treatment in Variola; and to the publishers, Lea Brothers & Co., for the uniform courtesy extended to us.

PHILADELPHIA, MAY, 1905.

W. M. W.
J. F. S.

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CHAPTER I.

VACCINIA.

Synonyms.—Latin, *vaccinia*, or *variola vaccinae* (Jenner); English, *cowpox* or *kinepox*; French, *la vaccine*; German, *Kuhpocken*, *Impfpocken*, *Schutzblättern*; Italian, *vaccinia*; Spanish, *vacuna*.

Definition.—Vaccinia is a disease communicable only by inoculation, and is characterized by one or more skin lesions, according to the number of insertions of the specific virus, running through the stages of papulation, vesiculation and pustulation, ending in desiccation and falling of the crusts at the end of the third week. The process is attended by slight febrile disturbance, and when completed confers immunity against smallpox.

History.—When Edward Jenner was pursuing his professional studies with his master at Sodbury, a young country woman, on hearing smallpox mentioned, immediately observed, “I cannot take that disease, for I have had the cowpox.” This incident created a deep impression in the mind of the young medical student, and may be said to have been the awakening impulse, which, after years of patient study and experiment, culminated in a discovery which has conferred the greatest benefits upon the human race.

To properly appreciate the life-saving value of Jenner’s discovery it is necessary to know something of the fearful mortality of smallpox in the prevaccination days. It was the most dreadful of all scourges, not excluding the plague, for that disease came but rarely, while smallpox was always present. Admiral Berkeley, chairman of the committee of the House of Commons (in 1802) to investigate the petition of Jenner for a Parliamentary grant, in an eloquent speech said:¹ “The discovery of Dr. Jenner is unquestionably the greatest discovery ever made for the preservation of the human species. It is proved that in these united kingdoms alone 45,000 persons die annually of the smallpox; but throughout the world what is it? Not a second is struck by the hand of time but a victim is sacrificed at the altar of that most horrible of all disorders, the smallpox.”

King Frederick William III. of Prussia stated in 1803 that 40,000 people succumbed annually to smallpox in his kingdom. The French Minister of the Interior, in reporting on vaccination in 1811, estimated that 150,000 persons died annually in France from smallpox. In

¹ Quoted by Baron. Baron’s Life of Jenner.

Russia smallpox is reported to have destroyed 2,000,000 lives in a single year.¹

The mathematician, Bernouilli, calculated that not less than 15,000,000 human beings died of smallpox every twenty-five years, which would give a yearly average of 600,000. Dr. Lettsom estimated that Europe alone claimed 210,000 victims each year. When to this number are added the deaths produced by devastating epidemics in Asia, Africa, and America, the aggregate estimate mentioned is seen to be conservative. The early records of the London Asylum for the indigent blind showed that three-quarters of the inmates had lost their sight through smallpox.² De la Condamine says that this disease destroyed, maimed, or disfigured the fourth part of mankind.

Traditions Concerning Cowpox Protection.—The fact that cowpox conferred protection against smallpox appears to have been noticed by dairymen in England as far back as the middle of the eighteenth century. It was observed by these people that when smallpox prevailed, those who had been accidentally infected by the matter exuding from certain sores, known as cowpox, which often appeared on the teats and udders of cows, resisted the infection of smallpox.

It is said that Benjamin Jesty, a Yetminster farmer, was the first person in England to employ cowpox virus for the purpose of protecting against smallpox. In 1774 he vaccinated his wife and children with matter taken from the teats of cows that had the cowpox. In about a week the arms became inflamed and considerable constitutional disturbance was present. The children were later inoculated with smallpox matter without result.

In Germany the protective influence of cowpox was known and practised prior to this date. Jobst Böse, a government official, called attention (*General Conversations of Göttingen*, part 39, May 24, 1769) to the fact that the protection conferred by cowpox against smallpox was recognized by reputable persons. He says: "I am reminded of the not unknown attacks of cowpox which were prevalent in this country, and to which to this day milkmaids are subject. In passing I wish to remark that, in this country, those who have had the cowpox flatter themselves to be entirely free from all danger of getting smallpox, and assert, as I myself, to have heard this same statement made by entirely reliable persons."³

In 1791 a school teacher by the name of Platt, who lived in Starkendorf, near Kiel, vaccinated several children of his landlord to protect them against a prevailing epidemic of smallpox. Several years later they escaped smallpox, although intimately exposed to the disease. He was prompted to perform this procedure by the popular belief concerning cowpox protection that prevailed in Saxony and in Holstein. A

¹ Woodville on Smallpox. Quoted by Baron.

² According to Sir William Aitken 90 per cent. of the cases of blindness met with in the bazaars in India are due to same disease.

³ Quoted by Kübler, *History of Smallpox and Vaccination*, Berlin, 1901. Kübler states that the writer of the above commentaries was a man with practical experience in farming.

Holstein farmer, Jensen by name, is also said to have employed prophylactic cowpox inoculation.

The same tradition, according to Humboldt, existed in certain parts of Mexico for many years, and similar statements are made concerning this belief in Baluchistan.

But it remained for Jenner to crystallize this half-forgotten tradition into a scientific theory, and then, by painstaking study and experiment, to establish its truth and prove it to the world.

Referring to the vaccinations performed prior to Jenner's time, Dr. Baron says: "They did not advance the knowledge or the practice of vaccination beyond what casual observation and popular rumor had rendered common in many districts; if indeed they ever took place (which I think more than doubtful) they were quite unknown to Dr. Jenner, and had it not been for his publication they never would have been drawn forth from their obscurity."

Early Practice in England.—Edward Jenner was born in the vicarage at Berkeley, in Gloucestershire, in 1749. He was the third son of Stephen Jenner, rector of Rockhampton and vicar of Berkeley. He exhibited an early taste for natural history, and as a boy interested himself in zoology and geology. After his scholastic education was finished he removed to Sodbury, where he became apprenticed to Mr. Ludlow, an eminent surgeon there, to be instructed in surgery and pharmacy. In 1770 he went to London to study medicine under the direction of the celebrated John Hunter, with whom he lived for two years.

In 1778 Jenner won the fellowship of the Royal Society, chiefly through his admirable essay *On the Natural History of the Cuckoo*. Despite his studies in natural history, the tradition concerning cowpox gave him much food for thought and was frequently mentioned by him in conversation with his friends.

After completing his course in medicine and locating in Berkeley, England, where dairy farming was common, Jenner gave close attention to this tradition, and it was not long until he was convinced of its reality. In medical coteries and societies he frequently expressed his belief in the protective power of cowpox, but his views on this subject were always regarded by his confrères as idle fancies of an overcredulous mind. On one or more occasions, in a certain medical society to which Jenner was a liberal contributor, the proposition was made, half earnestly and half jokingly, to expel him if he did not cease boring them with his absurd notions about the prophylactic power of cowpox. But the evidence he had already collected from various sources was too convincing to be set aside by such idle threats.

At length, after having devoted much time and thought to the subject, Jenner determined to inoculate into a human being the vaccine disease, and to test its efficacy by actual experimentation. James Phipps, a lad of eight years, has had his name made historical by having been the first subject to undergo the experiment. The virus used was taken from a vesicle on the hand of a milkmaid named Sarah Nelms, who had been accidentally infected while milking a cow. This vaccina-

tion was performed May 14, 1796, and was the beginning of Jenner's work which has made his name immortal. On the second day of July following Jenner proceeded to test the efficacy of this vaccination by inoculating the lad with smallpox matter taken from a patient suffering from that disease, but no result followed. At various intervals afterward, until this lad grew to be a man, he was inoculated with smallpox matter, in all as often as twenty times, and each time was found to be immune to that disease. It is no wonder, then, that Jenner arrived at the conclusion in his treatise on vaccinia that a single vaccination confers permanent immunity from smallpox.

The course of the vaccine disease in this case was very carefully noted by Jenner each day from the time the virus was introduced until the crust came off spontaneously, and, finding the affection was benign and wholly unattended by unpleasant results, he proceeded to subject others to the "new inoculation," as vaccination was called in those days. All his early cases were subjected to the same crucial test that was applied in the case of James Phipps, to prove the protective power of cowpox. It will thus be seen that the investigations of Jenner were conducted so carefully and thoroughly as to demonstrate most conclusively the value of his discovery before he ventured to publish his observations to the world. Quoting his own words: "I placed it on a rock, where I knew it would be immovable, before I invited the public to look at it."

It was not, therefore, until Jenner felt perfectly secure of his position that he ventured to detail his experiments and formulate his conclusions in a paper. This paper was prepared in 1797. It was Jenner's intention that this should first appear in the *Transactions of the Royal Society*, but this design was abandoned and the work subsequently appeared as an independent publication. In 1798 he published it as a modest brochure, entitled *An Inquiry into the Causes and Effects of the Variolæ Vaccinæ, a Disease Discovered in Some of the Western Counties of England, Particularly Gloucestershire, and Known by the Name of Cowpox*.

This publication at once attracted great attention from the medical profession in London and throughout England. Like all innovations, the "new inoculation" was viewed favorably by some, with distrust and skepticism by others, while a few resolved to test it for themselves.

Among the first in London to make use of the new discovery were Dr. George Pearson, physician to St. George's Hospital, and Dr. William Woodville, physician to the Smallpox and Inoculation Hospital. But the early work of these gentlemen tended to impair confidence in vaccination. They reported that vaccinia was attended with a generalized eruption more or less copious, resembling that of variola. When Jenner's attention was called to the matter he denied that such a result followed true vaccinia, and, on investigating the cases presenting this eruption, he found that Woodville had carelessly permitted the virus which he and Pearson were using to become contaminated with the

infection of smallpox. A considerable quantity of this virus was sent by these gentlemen to various parts of England and the Continent, and in many instances its use was followed by disastrous results. Foreseeing that vaccination was likely to be discredited by such carelessness, Jenner remonstrated against their procedure with some vehemence, but, instead of being listened to, was rewarded by the ill-will of Woodville and the lifelong enmity of Pearson.

When the news of Jenner's discovery had reached the various civilized countries of the world he became literally overwhelmed with correspondence. This grew to such immense proportions that he was forced to neglect his private work. He was, as he said, for many years the vaccine clerk of the world. All this involved a large expenditure of money, while he was reaping no substantial reward from his discovery. Finding that his small fortune was rapidly diminishing, some of his friends advised him to make application to the British Parliament for an honorarium. His claim was presented and ably supported. In the discussion it was contended that England owed to this worthy citizen not only her gratitude, but something more substantial, in consideration of his great discovery, which had already been the means of saving thousands of lives among her subjects, and had prevented untold suffering; and that the author of which was magnanimous enough to spend his time and fortune in spreading the blessings of his discovery throughout the entire world. The claim was opposed by some members of Parliament and by a few physicians, who should have been friends of the claimant. In the opposing argument it was contended that Jenner should have kept his discovery a secret long enough to grow rich by it before giving it to the world. To this Jenner replied: "While I had thus been employed in filling my own purse, should I not have indirectly been filling the churchyard with those slain by the smallpox?" Surely there could be but one answer to this question. And the sentiment it contains must have gone very far toward convincing Parliament that its author was a man worthy of the name of "great benefactor," and that the claims made for him as such could not be lightly set aside.

After the proposition to remunerate Jenner had been before Parliament a long time, and had been fully considered by a committee, a grant of £10,000 was voted him. This occurred in 1802. But considerable time elapsed before the money was paid, and its collection cost Jenner £1000. Feeling that this grant was very much too small for a great country like England to bestow upon her greatest benefactor, Jenner's friends petitioned Parliament again in 1807 for a second grant of £20,000. By this time the value of his discovery was better known and more generally appreciated, so that this grant was allowed with much less opposition than the first; and it was provided in the act that the amount should be promptly paid without any expense to the grantee.

Jenner labored incessantly to disseminate throughout the world a correct knowledge of this life-saving agent. In 1799 he published *Further Observation on the Variolæ Vaccinæ, or Cowpox*, in which

he carefully pointed out the difference between genuine and spurious cowpox.

It was not long before the merit of Jenner's discovery was universally admitted. In many instances the crowned heads of Europe set a good example by promptly accepting vaccination, and very soon arrangements were made to confer its blessings on the peasantry without cost. Honors were freely conferred upon Jenner from every European country, and he was regarded as the greatest benefactor the world had ever known. A letter from him served as the best passport one could have in traveling through foreign countries in time of war. As showing how highly he was esteemed, it is said that during the Napoleonic war two British subjects were held as prisoners by Napoleon, and that Jenner was importuned to write a letter requesting their release. The letter was read to Napoleon by Josephine, and when she mentioned the name of the writer, Napoleon exclaimed: "Jenner! Oh, we can refuse nothing to that man." And the prisoners were promptly released and permitted to return to England.

The Dowager Empress of Russia, Maria, wrote Jenner a most complimentary letter and accompanied it with the gift of a ring set in diamonds. In honor of the discovery she gave the name of "Vaccinoff" to the first child vaccinated in the Russian Empire, and settled an annuity on it for life.

In 1821 Jenner was further honored by being appointed physician extraordinary to the King of Great Britain.

The fame of Jenner spread throughout the entire civilized world. The most distinguished scientific bodies vied with each other in conferring honors upon him. From 1801 to 1822 Jenner received no less than twenty-eight diplomas from institutions of learning and scientific societies in every country of Europe and in the United States and Canada. Complimentary addresses were sent to him by public bodies and eminent individuals in every part of the world. In 1803 the corporation of London voted Jenner the freedom of the city, which was presented to him in a golden box. In the several succeeding years, Dublin, Edinburgh, Liverpool, and Glasgow conferred similar honors upon the illustrious, but modest physician.

Within a period of six years, eight medals were struck in Europe in honor of the great discovery. In 1804 one of the most beautiful of the Napoleonic series of medals appeared, commemorative of the emperor's estimate of the value of vaccination.

While Jenner's great renown rests upon the discovery and introduction of vaccination, he is to be credited with other notable scientific achievements, which would in themselves have entitled another to distinction. Dr. Baron briefly summarizes Jenner's scientific work in directions other than vaccination in this language: "In conjunction with Mr. Hunter he carried on experiments illustrative of the structure and functions of animals. With much industry and ingenuity he explained one of the most unaccountable problems in ornithology; he ascertained the laws which regulate the migration of birds; he made

considerable advances in geology, and in the knowledge of organic remains; he amended several pharmaceutical processes; he was an accurate anatomist and pathologist; he explained the cause of one of the most painful affections of the heart,¹ and advanced far in his investigations respecting the diseases of the lymphatic system, and the most numerous and extensive disorganizations to which animals are liable."

Jenner died of an apoplectic attack on January 26, 1823. Twelve days before he expired he wrote: "*My opinion of vaccination is precisely as it was when I first promulgated the discovery. It is not in the least strengthened by any event that has happened, for it could gain no strength; it is not in the least weakened, for if the failures you speak of had not happened, the truth of my assertions respecting those coincidences which occasioned them would not have been made out.*"

The Early Practice of Vaccination in Other Countries. FRANCE.—The practice of vaccination had traversed the wide expanse of the Atlantic and was in vogue in America before it was employed in the French capital. Valentin and Desoteux were the first French writers to call attention to the subject. Colladon, of Geneva, visited Paris on his return from England, and vaccinated some patients at the Salpêtrière. These vaccinations were unsuccessful. The failures were, however, unable to stem the growing tide of popularity of the new inoculation. Dr. Aubert was sent to London in 1800, as the representative of the National Institute and School of Medicine, to obtain all possible information and to secure virus. In the mean time, Liancourt commenced a subscription to establish a vaccine institute, and secured the moral and financial support of Lucien Bonaparte, then Secretary of the Interior. In January, 1800, Dr. Jenner's publication was translated into French by Count de la Roque. Five years later Napoleon demonstrated his confidence in vaccination by ordering all soldiers to be vaccinated who had not passed through smallpox.

SPAIN.—In the year 1800 the practice of vaccination reached Spain, through the efforts of Don Francesco Piguiem, who performed the first successful vaccinations in December of that year. Dr. Jenner's "Inquiry" was translated into Spanish in the early part of 1801. Spanish colonies were supplied with lymph through repeated arm-to-arm vaccinations of children on board ships.

INDIA.—Jenner endeavored to spread the benefits of his discovery into Asia and Africa. He sent his publications and large supplies of virus to India, but the boat carrying these was lost at sea. He was about to start a subscription to send another vessel when he received the tidings that Dr. De Carro, who had introduced vaccination into

¹ Jenner refrained from publishing his ideas on the subject of angina pectoris and the causative underlying pathology which he believed to be calcification of the coronary arteries, because his friend John Hunter was beginning to present symptoms of this disease. Jenner communicated his views on the subject to Mr. Cline and Mr. Home, but these gentlemen did not seem to think much of them. When Hunter died, Home wrote to Jenner and told him that the autopsy proved his view to be correct.

Vienna, had forwarded vaccine matter from that city to Constantinople, and thence to Bombay. In a short time from two to three thousand children were vaccinated in the latter city.

ITALY.—To Dr. Louis Sacco, of Milan, belongs the credit of having been one of the earliest and most successful disciples of Jenner. In 1801 he introduced vaccination into the Cisalpine Republic, which gave authoritative sanction to the practice and made him Director of Vaccination. Sacco labored with unwearied activity, and in a few years performed over 20,000 vaccinations. In many of these the virus was obtained from an animal with natural cowpox, which was discovered in Lombardy after a prolonged search.

Sacco was a warm admirer of Jenner, and the esteem was reciprocated by the latter. A letter written to Jenner in 1801 by Sacco begins thus: "It is to the genius of medicine, to the favorite child of nature, that I have the honor to write. The name of Jenner will be always beloved by all posterity," etc.

AUSTRIA.—The zeal and energy of Dr. De Carro were largely responsible for the early employment of vaccination in Vienna (1799). Besides being influential in disseminating this practice throughout other countries, De Carro interested his friend Count de Salm, who worked for the cause with the greatest energy and activity. This philanthropic nobleman distributed virus and literature gratuitously, and held out rewards to physicians who performed the greatest number of vaccinations. The good people of Brunn erected a temple which was dedicated to Jenner, and in which they annually held a festival to celebrate his natal day.

GERMANY.—Jenner sent virus to Prussia which was used to vaccinate the Princess Louisa. The admirable example set by the royal family excited a general confidence in the measure and led to its widespread employment. The king actively interested himself in vaccination, and founded a Royal Inoculation Institute in Berlin under the direction of Dr. Bremer. The latter collected funds to have medals struck commemorative of Jenner's discovery. These were given to the parents of vaccinated children when the latter were brought back for inspection on the seventh day. In 1799 Ballhorn and Stromeyer introduced vaccination into Hanover. The former gentleman translated Jenner's work into the German language. To Bavaria is due the distinction of being the first country to enforce compulsory vaccination (1807).

SWITZERLAND.—Vaccine matter was carried by Dr. Peschier to Geneva from Vienna, where he had studied the process under De Carro. The physician who labored most earnestly in Geneva in the cause of vaccination was Odier, who in 1801 wrote a memoir on the subject of cowpox.

RUSSIA.—In 1801 some of De Carro's ivory points and threads were sent from Breslau to Moscow, where the Russian court was assembled. Both Emperor Alexander and the Dowager Empress evinced a keen interest in vaccination and energetically promoted its employment,

The esteem in which the empress held Jenner may be judged from the following gracious epistle sent to him in 1802:

MONSIEUR JENNER :

The employment of vaccination in England having had the greatest and most fully attested success, I have hastened to imitate the example in introducing it in the religious establishments which are under my direction. I am pleased to report the success of my attempt, and to acknowledge my gratitude to him who has rendered this signal service to humanity. This motive prompts me, sir, to present to you the accompanying ring as an evidence of my sentiments of esteem and friendship, with which I am

Affectionately yours,

MARIE.

PAWLOSK, August 10, 1802.

DENMARK.—In the summer of 1801 Jenner gave some vaccine matter to Dr. Marcet for use in Copenhagen. His majesty, the King of Denmark, manifested a "personal solicitude for the welfare of his people," and, after receiving the report of an investigating commission on the subject, approved of all of the regulations suggested. The committee, of which Professor Winslow was a distinguished and active member, recommended legislation the enactment of which stamped out smallpox in Denmark for almost twenty years.

AMERICA.—The introduction of vaccination into this country marks an epoch of great importance. Smallpox had been present here almost from our earliest history. During the eighteenth century it was particularly rife in certain parts of the United States. The New England States attempted to prevent, by various legislative enactments, the introduction of smallpox into that section of the country. In some of these States variolous inoculation—a measure commonly practised during the middle and latter part of the eighteenth century—was prohibited by law. When persons residing in such localities wished to avail themselves of the advantages of smallpox inoculation they were in the habit of going to New York for the purpose of undergoing the disease in this way, and, after their recovery, returning to their homes. There was some inconvenience and considerable expense attending this procedure, but it was deemed wise by many to submit to this rather than run the risk of the indiscriminate introduction of smallpox into those States. In a large seaport town, however, such as Boston, where intercourse with foreign countries was constant, it was found impossible to exclude the disease by statutory law, so that the people of that city, thinking they would relieve themselves of the anxiety attending the constant risk of taking smallpox in the natural way, submitted by common consent on one occasion to a general inoculation. In order that the practice of inoculation should be conducted with as little risk as possible of the disease spreading by the natural transmission of infection, Dr. Benjamin Waterhouse, the first Professor of Theory and Practice of Medicine in Harvard College, published important rules and regulations governing the practice of the smallpox inoculation. Having thus been engaged in considering measures for restricting the spread of smallpox, it is not surprising that this physician should have been the first to urge upon the citizens of Boston the acceptance of Jenner's discovery.

Early in the year 1799 Waterhouse received from Lettsom, of England, a copy of Jenner's brochure of *Variolæ Vaccinæ*, and he became at once deeply impressed by the new and wonderful facts it contained. On March 12, 1799, he published in a newspaper of Boston a short communication, entitled "Something Curious in the Medical Line," in which he gave a brief account of the new discovery, referring to its marvellous protective power against smallpox, and predicting the incalculable benefits that the citizens of his own town and country would derive from it. "But," says Waterhouse, "this publication shared the fate of most others on new discoveries. A few received it as a very important discovery, highly interesting to humanity; some doubted it; others observed that wise and prudent conduct which allows them to condemn or applaud as the event might prove; while a greater number absolutely ridiculed it as one of those whims which rise to-day and to-morrow are no more."

Soon after this Waterhouse received from London a copy of Dr. Pearson's book (the second publication on vaccination) entitled *An Inquiry Concerning the History of the Cowpox, Principally with a View of Superseding and Extinguishing Smallpox*. At a meeting of the American Academy of Arts and Sciences, held in the University Building, and presided over by John Adams, then President of the United States, Waterhouse gave an account of the "new inoculation," read passages from Jenner's publication, and recapitulated from Pearson's book as much as he could remember, the book itself, he tells us, having been loaned and lost. The membership of the academy included the most cultured men of Boston, and the communication was received with interest and satisfaction by all; but none manifested so great an interest as the illustrious President himself, "who," as Waterhouse says, "to a profound erudition in letters and politics joins no small knowledge in the science of medicine."

Before the next quarterly meeting of the academy, Waterhouse received the third publication on the subject of vaccination, which was from the pen of Dr. William Woodville, physician to the Smallpox Hospital of London. This publication was entitled *Reports of a Series of Inoculations for the Variolæ Vaccinæ, or Cowpox, with Remarks and Observations on this Disease, Considered as a Substitute for the Smallpox*. In lieu of a paper which he had been asked to prepare for this meeting, Waterhouse read extracts from this publication. Having had as yet no experience in vaccination, not even having seen a case, he naturally failed to recognize the almost unpardonable mistake of Woodville. In his publication Woodville states that a large number of persons whom he "vaccinated" broke out during the course of the supposed vaccine disease with a vesicular eruption. Some, he says, had 200, some 300, some 500, and a few had from 1000 to 1500 vesicles. An infant at the breast died of convulsions on the eleventh day after the "vaccine matter" had been inserted, presenting at the time of death from 80 to 100 vesicles. The explanation of this unusual phenomenon is that Woodville first vaccinated a number of persons and then, three to five days afterward, inoculated them with variolous matter. The

result was that these persons were affected by both vaccinia and smallpox. Now, it was the virus taken from this source that produced the eruption in the cases just referred to. This mixed virus was distributed freely in London and elsewhere, and, as already stated, threatened for a time the reputation of Jenner's discovery. Woodville and some others regarded this generalized eruption as peculiar to vaccinia.

After Waterhouse had collected together a mass of evidence in support of the efficacy of vaccination, "too great," as he says, "to be resisted by any mind not perverted by prejudice," he began to seek the treasure. After several fruitless attempts to obtain the virus in an active state from England, he at length received some from Dr. Haygarth, of Bath, by a short passage from Bristol, and with it vaccinated successfully some of the younger members of his own family. This virus was received the latter part of June, 1800, and on July 8th he vaccinated one of his sons, Daniel Oliver Waterhouse, aged five years. So far as existing records show, this boy was the first person vaccinated in America.

Finding that the course of vaccinia in this child was typical, as compared with Jenner's description of the disease, he then vaccinated another son, aged three years, with virus taken from the arm of the first child; next a servant boy, aged twelve years, with some of the infected thread received from England; then an infant, one year old, and its nurse, both from the arm of the two-year-old boy. A few of the physicians of Boston and adjacent towns who felt an interest in the matter visited the subjects for the purpose of learning something about the new disease. The visits of these physicians gave rise to a malicious report that one of the Waterhouse children was so ill from the "new inoculation" as to require a consultation of several members of the profession. This was but the beginning of a long series of perversion of facts against which this worthy man had to contend in his work of introducing vaccination into Boston. A number of persons now applied to Waterhouse for the benefits of vaccination, but he declined to vaccinate anyone residing outside of Cambridge until he had proved that this new agent conferred protection against smallpox. He determined therefore to subject his children to smallpox inoculation.

Dr. Aspinwall, who was the physician in charge of the Smallpox Hospital, at once signified his willingness to assist in the experiment, and about two months after the vaccination of Waterhouse's children they were sent to the hospital and not only freely exposed to the infection of smallpox, but also inoculated with fresh matter taken from a patient. Finding the children resisted the disease absolutely when subjected to this most crucial test, Waterhouse exclaimed: "One fact in such cases is worth a thousand arguments."

Having now proved that vaccinia confers protection against smallpox, Waterhouse was ready and anxious to extend its benefits as widely as possible. He labored earnestly and persistently for the abolishment of smallpox inoculation, which was then commonly practised, and the adoption of vaccination in its stead. While he recognized the fact that inoculation had robbed smallpox of very many of its terrors, yet, like

Jenner, he looked confidently to vaccination to effect its entire extermination. For the purpose of showing the public the danger from smallpox, the benefit of smallpox inoculation, and the still greater benefit of vaccination, he published in the *Columbian Sentinel* a comparative view, somewhat figuratively stated. Thus:

<i>Natural Smallpox.</i>	<i>Inoculated Smallpox.</i>	<i>Kinepox.</i>
"A contagious disease; 1 in 6 who take it dies."	"Contagious; 1 in 300 dies."	"Non-contagious; never fatal."
"It is like an attempt to cross a dangerous stream by swimming, where 1 in 6 perishes."	"It is like crossing the stream in an old leaky boat, where 1 in 300 perishes."	"It is like crossing the stream on a new and safe bridge."

Waterhouse was desirous that vaccination should at first be placed only in careful hands; for he remembered that a few unsuccessful cases at the beginning of smallpox inoculation in Scotland deprived that country of the benefits of this measure for more than twenty years.

Jenner, in reply to a letter from Waterhouse informing him of the deterioration of the first supply of virus, and detailing certain unfortunate experiences in the hands of some physicians, wrote: "I do not care what British laws the Americans discard, so that they stick to this—never to take the virus from a vaccine pustule for the purpose of inoculation after the efflorescence is formed around it. I wish this efflorescence to be considered as a sacred boundary over which the lancet should never pass." This advice was so constantly given by Jenner, and was deemed of so great importance by him, that it became known everywhere as the "Golden Rule" of vaccination.

Early in the spring of 1801 Waterhouse received fresh supplies of virus from Jenner, Lettsom, and other friends in England. With additional information and fresh virus he began vaccinating again, and was rejoiced to find that the vaccine disease presented all the characteristics of the first case in his own family. He was now anxious that the benefits of vaccination should be diffused throughout this entire country. As he had received some months before a letter from Thomas Jefferson, President of the United States, in which this high dignitary manifested considerable interest in the subject, Waterhouse concluded that if the Chief Magistrate of the nation could be induced to take hold of the matter, vaccination would be introduced into the South more speedily and safely than by any other agency. The letter of the President contained not only an acknowledgment of the receipt of Waterhouse's pamphlet on the subject of cowpox, but a very complimentary reference to his humane work. The letter read as follows:

WASHINGTON, December 25th, 1800.

SIR: I received last night, and I have read with great satisfaction, your pamphlet on the subject of kinepock, and I pray you to accept my thanks for the communication of it.

I had before attended to your publications on the subject in the newspapers, and took much interest in the experiments you were making. Every friend of humanity must look with pleasure upon this discovery by which one evil more is withdrawn from the condition of man, and must contemplate the possibility that new improvements and discoveries may still more and more lessen the catalogue of evils. In this line of proceeding you deserve well of your country; and I pray you accept my portion of the tribute due you, and assurance of high consideration and respect, with which I am, sir,

Your most obedient, humble servant,

DR. WATERHOUSE, Cambridge.

THOMAS JEFFERSON.

In pursuance of his purpose, Waterhouse forwarded to the President, June 8, 1801, some virus, together with books and drawings descriptive of vaccinia, and requested that they be given to some careful and discerning practitioner—to his own family physician, if he preferred. He also sent a lengthy letter full of instruction as to the use of the virus, and courteously reminded the President that amidst the pelting storms of his adversaries Jenner had the countenance of his sovereign; that the Duke of York was a patron of the London Vaccine Institution; that Bonaparte took a lively interest in the dissemination of vaccination in France, and so did the German nobility at the Court of Vienna. He expressed the hope that the President of the United States would lend his influence to extend the blessings of the new discovery to the Middle and Southern States, believing, as he said, if it came from the hands of the Chief Executive of the nation it would make a greater and more favorable impression on the minds of the public.

The President's reply convinced Waterhouse that he had made no mistake in the course he decided upon. The virus which had been sent him was entrusted to a judicious and successful physician, but it failed to communicate the vaccine disease. So also did the second and even the third lot sent to the President by Waterhouse. A number of communications passed between these gentlemen, when at last Jefferson suggested that as the weather was warm the virus be placed in a small vial hermetically sealed, and that this vial be immersed in water in a larger one, which must also be hermetically sealed. The virus thus conveyed was used on some members of the President's family by Dr. Wardlaw, of Monticello, and proved successful. This occurred August 6, 1801. From his own family the President supplied Dr. Gantt, of Washington, with a small quantity of vaccine matter, and thus was the seed of vaccination planted at the capital of the United States.

All applications made to the President for virus received his careful attention. To him belongs the honor of sowing the seed of vaccination not only in the District of Columbia, but in Pennsylvania, Maryland, Virginia, and the States farther South. He studied the process of vaccinia so carefully that he was able to advise others as to the proper time for taking the virus. This period he fixed at eight times twenty-four hours from the date of vaccination. His advice in this matter, we regret to say, was frequently disregarded by physicians, who believed themselves wiser than he, but never without detriment to vaccination.

Waterhouse had the satisfaction of knowing that the virus which first proved effective in New York City came from him. To speak more definitely, it was taken from the arm of Governor Sargent's domestic, who had been vaccinated in Boston by Waterhouse, and thence was inoculated into several persons in New York City, on May 22, 1801, by Dr. Valentine Seaman. Vaccine virus first reached Philadelphia in an effective state November 9, 1801. It was forwarded by Jefferson, through Mr. John Vaughan, to Dr. John Redman Coxe, and was accompanied by a personal letter from the President, full of valuable instruction as

to its proper use. The first person who is said to have been successfully vaccinated in Philadelphia was Dr. Coxe himself.

Soon after Jenner's brochure was published there appeared in almost every civilized country in the world one or more supporters of the new discovery who adhered more faithfully than others to the teachings of the master, and consequently achieved distinction in this new field of beneficent work.

Waterhouse, of Boston; Sacco, of Milan; and De Carro, of Vienna, were the most faithful followers of Jenner. Of his many disciples, Waterhouse was probably the ablest and worthiest. It is, perhaps, not too much to say he was so regarded by the great benefactor himself. The published letters of Jenner clearly indicate his high esteem of this disciple. He well deserved the confidence of the master; for, single handed and alone, in his own city, he faithfully and earnestly defended and vindicated vaccination against the ridicule of the profession and the prejudice of the public for seven years, or until conviction became too strong for argument, and theoretical objections were forced to give way to stubborn facts. So earnestly, constantly, and successfully did Waterhouse devote his time and talent to the dissemination of vaccination in this country, and always so precisely in accordance with the teachings of Jenner, that he received the complimentary title of the "Jenner of America;" not, as might be supposed, by favor of the medical profession of his own country, but by the unanimous voice of the London Medical Society.

THE HYGIENE OF VACCINATION.

In order that a vaccination may pursue a perfect course and remain free of subsequent complications it is important that certain precautions be observed. These may be classified as follows: Care as to (1) purity of the vaccine virus; (2) condition of the vaccinée; (3) asepsis during insertion of the virus; (4) subsequent protection of the vaccine lesion.

Purity of Vaccine Virus.—Vaccine virus may be of human or bovine origin. Within recent years the use of calf-lymph has become generally and, indeed, almost universally adopted. 'The German government' in 1884 passed a law that vaccinations and revaccinations in the Empire of Germany be performed exclusively with animal vaccine.²

Humanized Virus.—In cases where it is necessary to employ humanized lymph, it is best taken from a vaccine pock from the fifth to the eighth day. Virus should only be used from a perfect, primary, vaccine vesicle containing clear or opalescent fluid. Where there is excessive inflammation or any other irregularity present, the vaccinifer should be rejected. The employment of the contents of lesions which have become

¹ Resolution of the Imperial Vaccine Commission of 1884; approval of the resolution by the Bundesrath, 1885.

² In Mexico humanized lymph is still extensively employed, and is preferred by the physicians of that country to bovine virus.

purulent is strongly to be condemned. Jenner's dictum was that lymph should never be taken from a lesion after the formation of the areola; this he regarded as the "golden rule of vaccination." The vaccine crust is inferior to direct arm-to-arm vaccination with fluid lymph. When a crust is employed at the present day it should be moistened with boiled water and rubbed up upon a sterile piece of glass.

The condition of health of the vaccinifer is of the greatest importance. When humanized virus is employed careful inquiry as to the health of the parental antecedents should be made. The subject from whom the vaccine is obtained should be in thoroughly good health. The greatest care should be taken to determine that the vaccinifer is free of hereditary syphilis. While the transmission of this disease by vaccination is extremely rare, its possibility is sufficiently well established to warrant every precaution being taken.

It is the custom to obtain vaccine virus only from young subjects; these are, of course, less apt to be suffering from certain transmissible diseases. It is well, however, that the infant vaccinifer should have reached the age of six months or thereabouts, so as to have passed the period at which evidences of hereditary syphilis usually make their appearance.

To obtain human vaccine lymph the vesicle, after having been previously cleansed with soap and boiled water, should be punctured in several places with a lancet and the droplets of lymph allowed to flow out. These are then transferred upon a clean lancet to the individual about to be vaccinated; or if the lymph is to be used later or employed upon some one at a distance, it may be collected in a sterile capillary tube. After the vesicle is punctured the tube is thrust through the opening, the lymph filling the tube by capillary attraction. When it is about two-thirds full the tube is withdrawn and the ends sealed by heating them in a Bunsen flame. The tubes should be kept in a cool place until used. To expel the lymph from the tube the ends should be broken off and the fluid blown out with a small rubber bulb.

At the present day we are chiefly concerned with *bovine lymph*. This material is employed in two different forms—as a lymph and as a vesicle pulp. Lymph, which is the clear fluid contents of well-developed vaccine vesicles, has been in use a long time. Pulp, which is a combination of the lymph and the interior epithelial structure of the pock, has more recently come into favor, and is at the present time regarded as possessing greater vaccinal activity than the clear fluid. Vaccine lymph is used either in the dry form upon strips of ivory or celluloid (so-called "dry points") or in sealed capillary tubes in the form of a glycerin emulsion.

There is a growing sentiment among the best observers in favor of the use of glycerinated lymph. This form of lymph has the sanction and endorsement of the British Royal Vaccination Commission. The method of preparation of dry and glycerinated lymph is elsewhere considered.

Condition of the Vaccinee.—There is nothing in the condition of a child that constitutes a sufficient contraindication to the performance

of vaccination, if there be liability of exposure to the infection of smallpox. We have vaccinated scores of children suffering from scarlet fever and diphtheria in the Municipal Hospital during the presence on the grounds of smallpox cases. We have never seen any untoward results from vaccinating these patients, but the vesicles have not always been as perfect as we would have liked to see them.

When smallpox is not prevalent it is proper for physicians to exercise discretion in choosing the time for the vaccination of an infant. There being no urgency, the medical adviser may wait until the child has reached a favorable age and is in good condition for the reception of the vaccine disease.

Age of Child.—In order that the proper protection against smallpox may be granted to infants it is advisable that they should be vaccinated during the first year of life. The vaccination laws of Germany require that every child be subjected to this measure before the expiration of the first year of life, unless it is contraindicated by reason of poor health. The age which is generally considered most appropriate is between *four and six months*, for at this period the child has not yet begun to be disturbed by the process of dentition. If there be danger of smallpox there is no reason to delay because of the tender age of the child. We have on a number of occasions vaccinated infants immediately upon their appearance into the world, and we do not recall any bad effects that have resulted from such early vaccinations. Indeed, we have been impressed with the very slight degree of constitutional disturbance that has attended such vaccinations. Where, however, no haste is necessary, we deem it well to wait for several months until the child becomes stronger and more accustomed to its mundane environment.

Health of the Child.—It is best to delay the performance of vaccination (provided smallpox be not prevalent) if the child is poorly nourished, or suffering from diarrhœa or vomiting, scrofulous glands, eczema, etc., or if the infant has been recently weaned or placed upon some new food. Vaccination of such children is prohibited by the regulations of the English Local Government Board. In general terms it may be said that when smallpox is not prevalent the physician may select such time for the vaccination of an infant as may find it in the best physical condition.

TECHNIQUE OF VACCINATION.

Vaccination being in a sense a surgical procedure, its performance must be guarded by those precautions of asepsis which at the present time apply to all chirurgical manipulations. Laboratory studies and practical experience have both shown that even in the most trivial of all surgical procedures—the introduction of a hypodermic needle into the skin—certain precautions as to bacterial cleanliness are necessary. Many years ago, before the days of bacteriology, this truth was not known and consequently proper care was not, as a rule, observed either in surgery or in the practice of vaccination.

Asepsis.—It is, of course, desirable that the vaccine lymph be free of foreign bacteria. In order that all wound infections may be avoided it is advisable that the arm of the vaccinée, the instrument to be employed, and the hands of the vaccinator be perfectly clean. Furthermore, the vaccine vesicle must be so protected as to prevent subsequent infection at the site of vaccination.

Disinfection of the Skin.—Some difference of opinion exists as to the thoroughness with which disinfection of the proposed vaccination area should be carried out. Some writers urge such a preparation of the skin as is practised prior to an ordinary surgical operation. Others believe that the use of strong antiseptics is to be avoided, inasmuch as they may destroy the activity of the vaccine material when placed upon the skin.

We would counsel the following technique: It is advisable for the patient to take a tub bath on or before the day on which the vaccination is to be performed, and to put on clean undergarments. (Unfortunately, it is difficult to have these measures carried out in the very people who most need them.)

The vaccination area, usually the arm, is to be thoroughly washed with potash soap and hot water, some friction being used so as to distend the cutaneous capillaries. Personally, we prefer to follow this cleansing with the application of alcohol, although in cleanly persons this is perhaps not necessary. The arm is then to be dried with sterile absorbent cotton, or, when this is not available, a perfectly clean towel. The operator may employ an ordinary lancet or a needle to produce the necessary abrasion. If the former is used it should be previously disinfected by boiling, immersion in an antiseptic solution, or thorough cleansing with soap and water or alcohol. It is perhaps better to employ a needle for the purpose, inasmuch as a new and clean one can be used for each vaccination.

The insertion of the deltoid muscle is the site usually selected for the introduction of the virus. The skin is made tense through the grasping of the inner side of the arm with the left hand. The epidermis is then abraded over an area of a third or a half inch; this is done either by vertical or cross scarification with a needle or simple scraping with a lancet or scalpel.

It is *important that the abrasion be not too deep*. The drawing of blood is to be avoided, inasmuch as it may float away the lymph and prevent absorption; it is further claimed that the deep scarification is more likely to be followed by an excessive degree of inflammation. It is not desirable to abrade deeper than is necessary to see the little reddish points which represent the loops of the papillary bloodvessels.

It is a matter of some importance to rub the virus well into the abraded surface. The hasty smearing of the lymph upon the arm with no further manipulation is probably responsible for a certain percentage of failures.

Some writers have advocated *vaccination by hypodermic or, rather, intradermic puncture*. This is accomplished by expelling the lymph upon the previously cleansed vaccination site, and then passing a thoroughly

sterile hypodermic needle obliquely through the skin over this area. Several punctures should be made within an area of 1 cm. square, but they should not be deep enough to draw blood. The puncture carries the lymph into the skin. The alleged advantage that little or no scar results from this method appears to us to be in reality a disadvantage—for the presence of a scar and its character constitute, as a rule, visible evidence of the amount of protection against smallpox which the individual enjoys. We therefore see no special advantage of this over other methods of vaccination.

It is best to allow the lymph to dry upon the arm by exposure to the air; this will ordinarily take from ten to thirty minutes. Where it is inconvenient to keep the arm bared for this time, there is no objection to protecting the abraded surface for a few hours with a loosely fitting shield made of pressed linen. It is important that no shield should be applied which congests the parts by peripheral pressure or which exerts any suction.

The vaccine vesicle when formed should be sedulously guarded against mechanical violence or injury. Nature provides an excellent protective covering for the vaccine wound—a hard, concrete, firmly attached crust. This crust is formed by desiccation of the vaccine pock. When the vesicle is ruptured by traumatism, some of the contents escape and form an irregular, friable crust which is easily detached, leaving an open wound which is liable to infection with pathogenic organisms.

Shields.—Various forms of shields have been devised to protect the vaccine lesion from injury and infection. Many of these have failed utterly of their purpose, and some have done actual injury by increasing the inflammation, and by rubbing off the scabs and thus producing open sores. Some writers condemn all shields; we have seen a few made of a light metal like aluminum which appeared to protect the vaccine lesions from the adhesion of the sleeve and from accidental injury without exerting any injurious compression. The use of such a shield, which can be easily sterilized, may be recommended. The application of a sterile gauze compress over the vaccine vesicle is also advocated; there is no objection to this save where the vesicle becomes ruptured, when the crust will adhere to the gauze and be torn off with its removal.

Patients should be advised not to allow the sleeve of the shirt or undershirt to rub against the vaccine vesicle. It is often a good plan to have a thoroughly clean piece of linen sewed into that portion of the sleeve which comes in contact with the vesicle. Caution should be given patients against rubbing, scratching, or otherwise fingering the vaccination scab; manipulation of this character is a fertile source of ulceration and late wound infection.

Number of Insertions.—It is the custom abroad to insert the lymph at several sites. When this is done the scarifications should not be too close, for fear of interfering with the vitality of the intervening skin, thus leading to sloughing. It is best to allow three-quarters of an inch

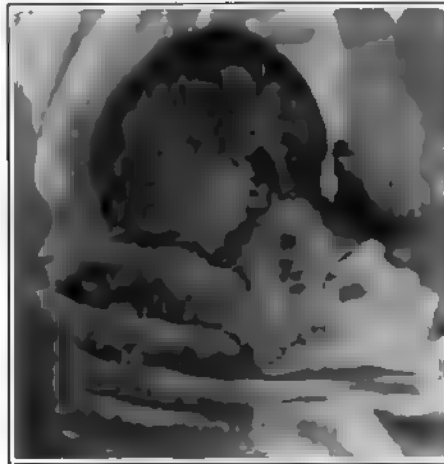
or an inch of healthy skin between the lesions. In this country it is the custom to make but a single insertion.

When a person has been exposed to the infection of smallpox it is well to insert lymph from two or three different tubes in different places, so that the fullest opportunity of inducing vaccinia may be offered. It is better that the patient should suffer from a sore arm than from smallpox.

SYMPTOMS AND COURSE OF VACCINIA.

Vaccinia in the human subject is always produced by inoculation. While the evolution of the vaccine lesion is a more or less constant one, yet a certain degree of variation will result according as the vaccination is performed with original cowpox virus, long humanized, or heifer-transmitted virus. These differences refer rather to the comparative

FIG. 1



Infant born of a variculous mother in the Municipal Hospital. Vaccinated on day of birth. Protection complete. Photographed on ninth day.

rapidity of the process, the size of the lesion, and the character of the crust and the resulting scar, than to any deviation in the evolution of the pock.

During the first two or three days after the insertion of the vaccine virus no symptoms are observed beyond those incident to the slight abrasion of the skin made by the operator's lancet. On the third or fourth day very faint redness may be seen around the site of the inoculation. This redness gradually increases while at the same time a distinct papule is formed, which becomes slightly more prominent by increasing in area rather than in height.

On the fifth day the lesion begins to be vesicular. This is usually observed first upon the margin of the inoculated area. The vesicle gradually increases in size, and the lymph that it contains is at first thin and perfectly transparent. On the eighth day the vesicle reaches its

greatest perfection; it is then considerably elevated above the surface of the skin, and presents a "pearly" appearance, although at times the vesicle is yellowish. When examined closely it will be found to have, even at an early stage of its development, an umbilicated form similar to that seen in the vesicle of variola. The peripheral portion of the vesicle is bulging and prominent, whereas the centre is depressed.

About this time there appears around the vesicle an inflammatory band or areola. This is most intense in the immediate neighborhood

FIG. 2



Vaccine vesicles on the eighth day, showing little or no surrounding inflammation.
Infant vaccinated at birth, owing to exposure to smallpox.

of the vesicle, gradually merging into the normally tinted skin. During the ninth and tenth days the redness increases; streaks of redness often extend a considerable distance from the lesion. Occasionally the cellular tissue becomes involved in the inflammatory process, producing a swelling and hardness of the skin of the arm. The glands of the axilla, when the vaccination is performed upon the arm, frequently become enlarged and painful.

At the same time mild constitutional symptoms make their appearance. Slight rigors sometimes occur, followed by moderate elevation of temperature. It is not often that the temperature rises more than one, two, or three degrees above the normal. There are apt to be malaise, impaired appetite, and disturbed sleep; but none of these symptoms continue very long. In recording very carefully the constitutional disturbance observed in his first case of induced vaccinia, Jenner says: "On the seventh day he (a boy aged eight years) complained of uneasiness in the axilla, and on the ninth he became a little chilly, lost his appetite, and had a slight headache. During the whole of this day he was perceptibly indisposed, and spent the night with some degree of restlessness, but on the following day he was perfectly well." It cannot be doubted, however, that many children pass through the regular course of vaccinia without any apparent systemic disturbance; our experience leads us to believe that in very young infants, particularly those but a few weeks old, the febrile reaction is less pronounced than in older children. At times both the constitutional and local symptoms of vaccinia are very severe, especially in secondary vaccinations.

It occasionally happens in severe cases of primary vaccinia that a cutaneous eruption appears at about the tenth day of the disease. This eruption consists of a macular erythema similar to but flatter than the measles eruption. The efflorescence may be comparatively limited in extent or it may cover almost the entire body. On account of its not infrequent association with the vaccine process it has been called *roscola vaccinosa*. An analogous and almost identical eruption, designated *roscola variolosa*, is occasionally seen in modified cases of smallpox just before the appearance of the papules. These eruptions seldom continue longer than two or three days.

On the eleventh or twelfth day of the vaccine process, the pock begins to fade. In its declining stage its contents become opaque, desiccation appears in its centre, and the areola shades off into two or three concentric circles, varying in color from a pale red to a deep red or livid tinge.

By the fifteenth day desiccation is usually completed, although the crust does not fall off, nor can it be easily removed until the end of the third and frequently not until the end of the fourth week.

FIG. 8

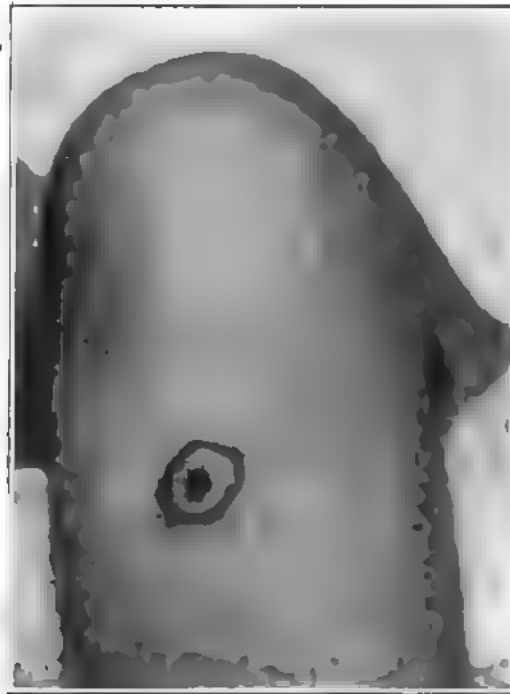


Vaccine vesicle upon the seventh day areola just beginning

The completed crust is of a mahogany color, rough on its exterior, thin at its centre and periphery, with a thick, circular ridge between. The scar is at first red, but in the course of some months becomes paler than the surrounding skin. It is pitted or foveolated, and not infrequently presents an elevated centre from which cicatricial bands radiate to the periphery. A perfectly typical scar looks as if it had been stamped into the skin with a sharply cut die.

As the analogy between cowpox and smallpox is in most respects very close, and as variola frequently differs in the duration and severity of its local manifestations, so also it must be expected that the local lesions

FIG. 4



Vaccine vesicle upon seventh day, showing beginning areola. Patient was suffering from scarlet fever. Vesicle shows some irregularity in form.

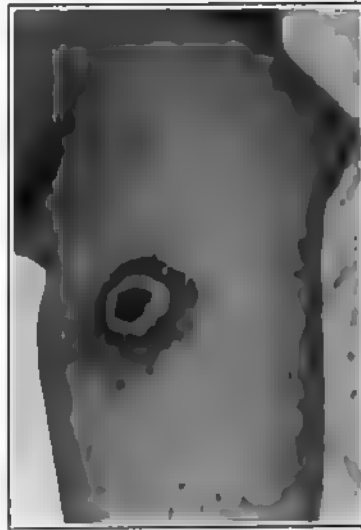
of vaccinia will not invariably follow the typical course just described. In some cases the course of the disease is undoubtedly shorter and milder, while in others it is longer and more severe. It is essential, however, that the pock pass through the stages of papule, vesicle, and pustule. Likewise, the constitutional symptoms are not uniform; they may not be present at all, or, if present, may be so mild as to pass unobserved.

Tardy Vaccinia.—Occasionally a retardation of the vaccine process is observed; usually this does not amount to more than a delay of two or three days in the development of the vesicle. In such cases vesicula-

tion is observed upon the seventh or eighth day, and the areola does not develop until the tenth or eleventh day. The development of the pock may be postponed even longer. We have seen patients present no evidence of vaccinal reaction until a week or ten days has elapsed; on such occasions one is apt to conclude that the vaccination is a failure, when, lo and behold, the lesion assumes activity and passes through the normal development of the vaccine pock. We have observed the vesicle to appear as late as one month after the inoculation was performed and then pursue its normal course. Instances have been reported in which the retardation has been much longer.

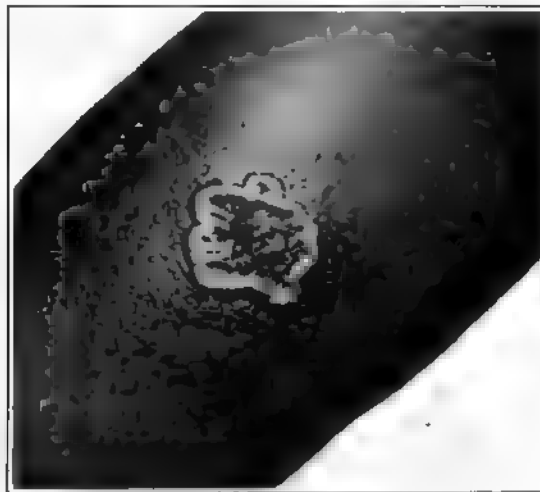
It not infrequently happens that fresh lymph inserted into an individual who has been some days previously vaccinated with apparent failure will often awaken activity in the old sites of inoculation, and thus the first attempt and the more recent vaccination

FIG. 5



Vaccine vesicle upon ninth day, showing more pronounced areola. Same patient as Fig 4.

FIG. 6



Vaccine lesion in a mulatto on the tenth day, showing some irregularity in the shape of the vesicle.

will both exhibit lesions which run their course at the same time. Bousquet reports a case in which such a revival of a dormant vaccination is said to have occurred three weeks after the insertion of the virus.

FIG. 7



Vaccination performed after exposure to smallpox, showing vaccine lesions about the fourteenth day. Patient was almost completely protected, developing but a few variolous lesions.

FIG. 8



Hard, concrete, umbilicated vaccinia crust on a patient exposed to smallpox and vaccinated eight days before the variolous eruption appeared. Considerable modification of the exanthem.

A tardy development of the vaccine lesion occurs more commonly with the use of dry virus than with a liquid lymph. A retardation of cowpox in a healthy individual does not in the least impair its protective power provided it runs a regular course. It is evident, however, that a tardy development of the vesicle in one who has been exposed to smallpox might result in most serious consequences, in that the individual might develop variolous symptoms before the vaccine vesicle is sufficiently far advanced to confer protection.

Precocious Vaccinia.—This modification of the normal course of vaccinia is much rarer than retardation of the process. An acceleration of the cowpox vesicle occasionally occurs, the development being hastened by twelve or twenty-four hours. In such cases the usual appearances of the eight-day pock are manifest on the seventh day. These remarks apply, of course, to primary vaccinations; in secondary vaccinations the process is not infrequently hastened and shortened.

A very hasty development of vaccinal reaction in a primary vaccination should direct attention to the possibility of a spurious result, as such lesions not infrequently appear early after the insertion of the lymph.

Accessory or Supernumerary Vesicles.—It occasionally happens that a moderate number of supernumerary pocks are seen in the neighborhood of the vaccine inoculation. Whereas but one abrasion may have been made upon the arm, we now and then observe two or more vaccine lesions develop. At times the accessory pocks never pass beyond the stage of papulation, but at other times they undergo the usual evolution. The fact that such additional pocks observe a predilection for the immediate neighborhood of the original inoculation suggests that they may have resulted from absorption of virus through minute and unobserved abrasions. It is contended by some writers that they are due to transmission of the virus through the lymphatics, inasmuch as they commonly develop at a time when the primary vaccine vesicle begins to fill with lymph. In rare cases vesicles may develop upon other parts of the body, but to this reference will be made later.

Bryce's Test: Reinsertion of Vaccine Matter Five Days After a Successful Vaccination.—Bryce, of Edinburgh,¹ demonstrated the fact that a fresh insertion of lymph made at any period not later than the fifth day from the successful insertion of vaccine virus into a child's arm would take effect as surely as if no previous vaccination had been performed. The later vesicles will overtake in their course the vesicles first made, and will mature and fade at the same time with them, although they will be smaller in size. For instance, if some active vaccine lymph be inoculated four or five days after a first vaccination, the vesicles of the second insertion will, by the tenth day of the primary vaccination, mature and be surrounded by an areola, although they will have but the size of a five or a six-day vesicle. If the second insertion is delayed beyond the fifth day, there will be either no result at all or merely the formation of a hard papule. Bryce advocated the practical

¹ *Practical Observations on the Inoculation of the Cowpox*, Edinburgh, 1802; second edition, 1809.

employment of lymph reinsertion to test the efficacy of the protection conferred by the original vaccination. He argued that there might be a perfect local vaccine result, without such a systemic impression as to confer absolute immunity against smallpox; he thought that by the routine reinoculation of lymph on the fourth or fifth day the existence of the constitutional protection might be tested. This practice, which has become known as Bryce's test, has not been accorded much endorsement, and has fallen into disuse. It has, however, a scientific interest, for it is the analogue of the accidental autovaccination which occurs in natural cowpox, as a result either of movements of the cow or the manipulations of the milker.

Spurious Vaccination.—It is deemed necessary to refer to a spurious variety of vaccine lesion which has grown more frequent of late years, namely, the red *raspberry excrescence*, as it is commonly termed. This growth, when seen, usually appears from three to seven days after the introduction of the virus, beginning as a red elevation at the site of inoculation, quite similar in appearance to the papule of true vaccinia, but instead of advancing to the vesicular stage it remains hard, dense, bright red in color, and nodular in form, looking not unlike a small *nævus*. A thin, friable crust forms on its surface, but when this is removed the lesion continues to present the same general appearance just described. It is very persistent, remaining usually for weeks or even months; no areola forms around it at any time, and it is not followed by a scar.

This peculiar excrescence was described by some of the earlier writers on vaccination; but during the long period in which humanized virus was used exclusively, it was not observed. Since the introduction and general employment of animal vaccine virus it has frequently been seen. It seems, therefore, that it occurs as the result of inoculating the human subject with some unknown form of inert or non-specific material, taken from a vaccinated bovine animal. That this is a spurious form of the vaccine disease, and utterly devoid of protective power against either variola or vaccinia, the writers have had ample opportunities of proving.

The vaccine vesicle sometimes runs an entirely irregular course. In such cases it begins with itching and irritation; instead of being flat and umbilicated, the vesicle is acuminate or conical. The fluid is commonly opaque or yellowish instead of being a clear lymph; as a result the characteristic pearly lustre of the vesicle is absent. An irregular areola often develops about the fifth or sixth day; several days earlier, therefore, than in the normal vaccine vesicle. A small scab forms which usually drops off about the tenth day.

Not infrequently the vesicle ruptures early, giving issue to a thin, yellowish fluid which dries in the form of a friable crust. This may become detached and succeeded by a second crust, which results as the first from the desiccation of the exuding material.

Sometimes the local reaction is less pronounced, the site of vaccination inflaming early and scabbing within a few days, so that at the end of a week the process has entirely terminated.

Bousquet, quoted by Trousseau, says: "True cowpox hardly begins to show itself at the end of the third day; but the false is much earlier, and may be seen from the first to the second day after the introduction of the virus, a circumstance which from the first constitutes a distinction between the two affections. False cowpox sometimes shows itself as a small pimple, which goes on increasing until the fourth or fifth day. On the sixth or seventh day its progress becomes arrested, it grows pale, and dries up. At other times it advances farther, always preserving in its rapid development a conical or globular shape, which I look upon as an unerring sign of false, as the flattening and central depression of the pock are signs specifically characteristic of the true. . . . The false pock is sometimes red and sometimes yellowish. It never assumes the brilliant, silvery lustre which distinguishes the prophylactic cowpock."

Such lesions as those described, of course, utterly fail to give any protection against smallpox. Inaccurate observers have not infrequently regarded such "sore arms" as successful vaccinations, and have been surprised to see such individuals later contract smallpox.

We have on several occasions observed smallpox develop in individuals who have had local reactions which were regarded by themselves, and in several instances by their physicians, as genuine "takes." We recall the case of a stout woman of thirty years, who had been vaccinated without result some years previously, and who was vaccinated one month before admission to the Municipal Hospital. She informed us that there had been some local reaction, and the physician in attendance had been for a time in doubt as to whether there had been a successful "take" or not, finally deciding in the negative. The patient developed confluent smallpox and died in ten days. From an examination of the arm on admission we were convinced that the result had been spurious.

A young man, aged twenty-five years, was vaccinated for the first time about Christmas of 1901. He stated that the vaccination was inflammatory from the outset. A vesicle was rapidly formed, and later an areola and axillary tenderness developed. A reddish crust remained upon the vaccine site for a period of three weeks. The physician in attendance regarded the sore as a genuine "take." The patient was admitted to the hospital on February 6, 1902, about six weeks later, with a malignant type of confluent smallpox, to which he rapidly succumbed. Examination of the arm of this patient upon admission to the hospital showed a brownish-red stain, but no scar whatsoever. In this case, in which the vaccination was a primary one, its spurious character was evidenced not only by the atypical development of the vesicle and the absence of a characteristic resulting scar, but by its signal failure to protect against smallpox.

INSUSCEPTIBILITY TO VACCINATION.

Occasionally persons are encountered who exhibit an insusceptibility to the virus of vaccinia. The number is, doubtless, much smaller than is commonly believed, for one or two unsuccessful attempts at vaccination are often construed to indicate an insusceptibility to the infection.

Gregory says: "The proportion of mankind who exhibit this singular idiosyncrasy is very small. I have seen thirty or forty such cases in the course of my life. It would be very interesting to determine whether this constitutional inaptitude to cowpox denotes a like inaptitude to receive and develop the variolous poison. In the few cases which I have seen, where inoculation was subsequently tried, the insusceptibility was proved to extend to both poisons, but I have read of instances of an opposite kind."¹

Of upward of 9000 vaccinations performed at the Blackfriars' station of the National Vaccine Establishment during a period of about ten years following 1859, there was but 1 case which on a second trial was unsuccessful. In this case a third attempt was made, but the child was not brought back for inspection, and the result, therefore, could not be ascertained.²

There is strong reason to believe that a person may be immune to vaccinia at one period, but later develop a susceptibility to the vaccine disease. Such instances of temporary absence of susceptibility are not particularly rare. Gregory believed that such failures might be attributed to atony of the absorbent system in children exhibiting "slowness of dentition, imperfect ossification of the head, emaciated aspect of the body," etc.; in other words, evidence of rachitis.

It has also been claimed that the existence of certain cutaneous diseases, the eruptive fevers, etc., produces a temporary immunity against vaccinia. This statement scarcely coincides with our own personal experience; owing to the fact that children suffering from scarlet fever and diphtheria are treated in the Philadelphia Municipal Hospital upon the same grounds as the smallpox patients, we have been obliged to vaccinate scores and scores of such patients. We have found that the vaccination is received almost if not quite as uniformly in children with scarlet fever and diphtheria as in those enjoying good health.

In Scotland (1864-65) 1 of every 200 children proved refractory to three successive vaccinations, thus entitling them to a certificate of insusceptibility. Doubtless many of these children would have responded to vaccination had it been tried some years later.

During the period that vaccination was performed from arm to arm, successes were so uniform that a person who resisted three attempts on three successive weeks was assumed to be temporarily insusceptible. Such an inference would scarcely be warranted with the employment

¹ Lectures on Eruptive Fevers, 1851, p. 244.

² Mentioned by Seaton, Handbook of Vaccination, 1868, p. 196.

of bovine lymph, particularly when used in a dry state. Dr. Spalding, Chief Medical Inspector of the Chicago Board of Health, writes that he has known eight, ten, and in one instance—in the practice of a colleague—thirteen attempts at vaccination to be made before a successful result was obtained.

Insusceptibility to vaccinia, or rather failure of result after repeated attempts to vaccinate, does not of necessity indicate an insusceptibility to smallpox. We recall to mind a young physician who had been repeatedly vaccinated in childhood and youth without successful result, who on brief exposure to a mild case of variola contracted a severe attack of confluent smallpox. We have also in mind a young woman who fell ill with hemorrhagic smallpox, although she had had seven unavailing trials at vaccination made upon her, three of which were performed within a year preceding the attack of smallpox.

The late Mr. Spurgin, of Northampton, forwarded some years ago to the Epidemiological Society the particulars of a case in which in 1825, a boy fourteen years old, whose family was greatly opposed to vaccination, was inoculated with variola six or seven times without any result, that disease being then prevalent. The father then allowed vaccination to be tried, and the boy was vaccinated six or seven times, but equally without effect. About a year after, when at a distance from home, he contracted natural smallpox of the discrete kind, and went through the disease favorably (Seaton).

REVACCINATION.

Experience has demonstrated the fact that in a certain number of persons the protection from vaccinia in infancy is permanent, while in others it gradually diminishes, and after the lapse of a number of years may become entirely extinguished. The extinction of immunity is evidenced by the large number of persons in adolescent and adult life who are susceptible of revaccination; also by the observation that in all epidemics of smallpox a large proportion of the cases occur among persons who were vaccinated in infantile life. The statistics of smallpox hospitals in this country and in England show that from 41 to 78 per cent. of the admissions are postvaccinal cases. It is very difficult to determine the proportion of persons vaccinated in infancy that fail of permanent protection, but it is believed to be not far from 75 per cent. Some years ago a very careful observation in a certain American city showed that of 2362 persons revaccinated with reliable virus (no child under twelve years old with a good scar being included in this number) 77.1 per cent. were susceptible to some form of vaccinia.

We have no means of ascertaining the age or period of life at which the protection from vaccinia in infancy is liable to diminish or cease entirely, save by applying the test of revaccination or by noting at what age after primary vaccination any considerable number of persons suffer from smallpox. Data tending to demonstrate the latter may be found in the following table:

		Cases.	Deaths	Percentage of deaths.
Under one year	Unvaccinated	134	86	64.18
	Vaccinated	2	0	0.0
One to seven years	Unvaccinated	676	280	41.42
	Vaccinated in infancy, good scars	11	0	0.0
	“ “ “ fair “	11	1	9.09
	“ “ “ poor “	16	1	6.25
	Total number vaccinated	38	2	5.26
Seven to fourteen years	Unvaccinated	320	87	27.19
	Vaccinated in infancy, good scars	61	2	3.28
	“ “ “ fair “	24	2	8.83
	“ “ “ poor “	64	9	14.06
	Total number vaccinated	149	13	8.72
Fourteen years and upward	Unvaccinated	1742	868	49.83
	Vaccinated in infancy, good scars	1864	138	7.4
	“ “ “ fair “	894	114	12.75
	“ “ “ poor “	1240	318	25.24
	Total number vaccinated	3998	565	14.13

Among over 9000 cases of smallpox admitted to the Municipal Hospital of Philadelphia during the past thirty-four years we have admitted only two vaccinated patients under one year old. One of these was a child eleven months old who had been vaccinated two months previously and showed a good scar. The eruption consisted of only six small vesicles, and the child's health was scarcely at all disturbed. The other patient had the disease so indistinctly marked that it was almost impossible to feel certain of the diagnosis of varioloid. An exceedingly modified form of smallpox was occasionally seen among well-vaccinated children between the ages of one and seven years, but no deaths occurred except where there was a serious complication. The child that died, whose case is classified under the head of "fair scars," was a foundling about a year old, badly nourished and very feeble, with a disordered digestion. The eruption consisted of only a very few small vesicles. Death really resulted from inanition. Very little need be said of the cases classified in this age period under the head of "poor scars," as the vaccination in them had been in good part either imperfect or spurious.

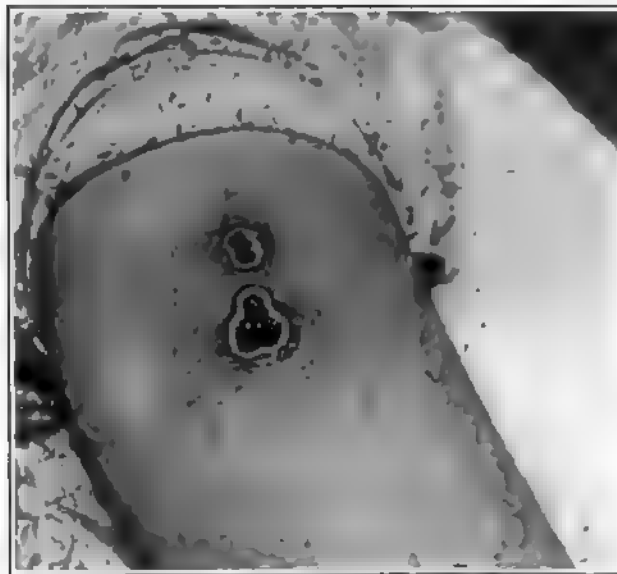
The query is often asked, What constitutes a successful revaccination? This is a question about which there is considerable diversity of opinion. Many believe that, unless the vesicle and areola observe the course of true vaccinia, the effect is merely local and devoid of prophylactic power. But it is evident on a little reflection that there is no more reason why we should expect the vaccine disease produced by revaccination to be typical than we should expect smallpox after vaccination to run the typical course of variola vera. If there be modified smallpox or *varioloid* after vaccination, so should there be modified vaccinia or

vaccinoid. From these premises the conclusion may be deduced that as varioloid confers immunity against a recurrence of smallpox, so also does the modified form of vaccinia resulting from revaccination remove from the individual whatever susceptibility to the disease may be present.

It is frequently a matter of great difficulty in revaccinations to distinguish between irritative local reactions and lesions which result from the specific action of the vaccine principle.

Course of Revaccination.—The degree of perfection of the vaccine lesion produced by a revaccination obviously depends upon the extent of vaccinal susceptibility remaining in the individual. Where the protection conferred by the primary vaccination is still complete no specific result at all is produced by a second insertion of vaccine lymph. Such

FIG. 9



Revaccination in an adult, showing vesicles upon the eighth day.

a condition obtains in the vast majority of children who have been vaccinated in infancy. As time goes on there occurs in most vaccinated individuals a gradual depreciation in the character of the vaccinal protection, and, *pari passu*, an increasing susceptibility to revaccination. In some cases the deterioration of the vaccinal influence may go on to complete extinction, in which event the subject offers an unmodified susceptibility to revaccination, and a vaccine lesion results which is almost or quite indistinguishable from a primary vaccination. This occurs in a comparatively small number of people, and chiefly in adults whose primary vaccination was performed many years before. In the vast majority of persons the phenomenon of a typical vaccinia can only be produced once in a life-time. More commonly the vaccine lesion is much modified. There may result merely a papule or more often

an acuminate vesicle with an irregular areola which runs a rather rapid course. There is often considerable itching and not infrequently marked constitutional disturbance. Severe systemic symptoms appear to develop more often in revaccinations than in primary vaccinations, although in many cases they are absent altogether.

Hervieux, in 1893, read before the Paris Academy of Medicine an article on vaccinoid, in which he classifies the modified vaccine lesion as follows: "There are three types of vaccinoid, dependent upon the extent to which the weakening of the immunity has advanced:

"1. At the point of inoculation there appears a pink papule hardly at all elevated above the surrounding integument, and without any areola; it disappears at the end of a few days, leaving no scar.

"2. There forms an acuminate papule, larger than that seen in the first type of vaccinoid, redder, more distinctly visible, surmounted by a little vesicle at its point, surrounded by a faint areola, and leaving after desiccation a little scab, which falls soon without the formation of a cicatrix.

"3. The vesicle is more distinct, the areola is more pronounced, the scab is larger and more adherent, and leaves behind it a cicatrix, which, however, disappears in the course of time. These evidences of vaccinal action are usually accompanied by considerable itching, but there is no fever and the process confers immunity."

Hervieux states that vaccinoid transmits by inoculation true vaccinia.

The above classification does not take cognizance of the well-developed vaccine results which we not infrequently encounter in individuals in whom the immunity conferred by the primary vaccination has become almost completely exhausted. In these cases there may be a well-formed vesicle with central umbilication surrounded by an areola, but the course of the disease is more rapid and shows some degree of modification.

It is seen from the above that the vaccinal result in revaccination is most variable, and that there is no standard in an individual case. The criteria upon which the result in any given instance might be judged are obscured by the indeterminable degree of existing vaccinal susceptibility.

It is, therefore, often a matter of difficulty to know whether the result in a revaccination is specific and genuine, or spurious. Such doubt, however, should not extend to the judgment of a primary vaccination. Jenner's description of the course of vaccinia constitutes an ever-important guide. Any result which deviates to any considerable extent from the description of primary vaccinia given by Jenner should not be regarded as genuine. Therefore, while the modified results referred to might be credited with being the specific results of revaccination, they should never be regarded as genuine in primary vaccinations.

We are convinced of the fact that many local reactions similar to those described by Hervieux are not genuine "takes." Such lesions not uncommonly show an unusual degree of inflammatory action, even as early as the second or third day. Upon this area there frequently

PLATE I.



Secondary Vaccination of Doubtful Character (Twelfth Day)
followed by a Slightly Pitted Scar.

springs up with surprising rapidity a more or less conical or globular blister, instead of a typical vesicle. This epidermal elevation is thin-roofed, and ruptures readily, giving exit to a thin, irritating fluid, which speedily dries in the form of a friable, yellowish crust, the exudation continuing to ooze out at the margins. After shedding of the crust there is left a faint scar, which is devoid of the characteristics of a true vaccine cicatrix.

The proof that many of these results are spurious is in the fact that they do not protect against smallpox. Numerous cases have been reported in which lesions erroneously interpreted as genuine conferred only a fancied and not a real security against smallpox. Glycerinated bovine lymph manufactured by a certain firm in 1900 was extensively used in some of the Southern States with alleged large percentage of successes.¹ Some of the vaccinated persons on being exposed to smallpox a short time afterward contracted the disease. The vast majority of the persons upon whom this lymph had been used were subsequently successfully vaccinated with virus from another source.

The following case demonstrates the difficulty in estimating the genuineness of revaccination. In the spring of 1902 a trained nurse, who had been in attendance upon a private patient suffering from smallpox, was brought into the Municipal Hospital with a mild attack of varioloid. She presented upon her arm a poor mark from a vaccination in childhood. She had been revaccinated a number of weeks before admission with dried virus upon an ivory point. According to her description, a vesicle formed in from two to four days. This itched considerably, and later became surrounded with an areola the size of a silver half-dollar. The axillary glands were distinctly tender. The crust remained upon the sore for a few weeks. The nurse and the physician in attendance regarded the result as a successful vaccination. Upon admission to the hospital the patient exhibited a reddish-brown stain at the site of vaccination, but no true scar. We were convinced that the result had been spurious.

Value of Revaccination.—As to the value of revaccination there can be no question. It is the logical complement of vaccination. Bousquet says very truly that there never has been an epidemic of smallpox since the general employment of Jenner's discovery which has not proved the virtue both of vaccination and revaccination. He adds: "The success of revaccination is at the same time the effect and the proof of the wants of the system; . . . when it succeeds, it not only proves that the protective power of vaccination is diminished, but it supplies a remedy for this diminution."

No person should be regarded as having been revaccinated if the secondary vaccination has not been followed by a successful result. Where a revaccination, unproductive of result, is successful when again tried after a brief period of time, the probabilities are that the first failure was due to the employment of inert lymph or imperfect technique

¹ Reported by Dr. F. J. Runyon, Clarksville, Tenn.

rather than to insusceptibility on the part of the subject. The failure of a revaccination should not be interpreted as an evidence of certain immunity, but the process should be repeated with carefully selected virus two or three times in order to eliminate all sources of error. When the character of the resulting lesion in a revaccination is doubtful, the procedure should be repeated, particularly if the individual is liable to be exposed to the infection of smallpox.

Does insusceptibility to revaccination indicate immunity against smallpox? Jenner in his "Inquiry" says: "Although the cowpox shields the constitution from the smallpox, and the smallpox proves a protection against its own future poison, yet it appears that the human body is again and again susceptible of the infectious matter of cowpox." Instances are given of the cowpox twice or thrice taken by persons who could not be variolated either by inoculation or exposure.

Our own experience would lead us to believe that in the great majority of cases insusceptibility to a revaccination carefully performed with good lymph means insusceptibility to smallpox, and *vice versa*. The English Royal Vaccine Commission makes the following conservative statement: "No doubt the want of success (in a revaccination) shows, if the operation has been thoroughly performed, that the person is at the time insusceptible to the virus, *and it may be to the virus of smallpox also.*"

Vaccination After Smallpox.—In one of his later publications Jenner remarks: "Although the susceptibility of the virus of the cowpox is for the most part lost in those who have had the smallpox, yet in some constitutions it is only partially destroyed, and in others it does not appear to be in the least diminished. By far the greater number on whom trials were made resisted it entirely; yet I found some on whose arms the pustules from inoculation (vaccination) was formed completely, but without producing the common efflorescent blush around it, or any constitutional illness, while others have had the disease in the most perfect manner."

We presume that Jenner in this essay refers to vaccination performed a number of years after an attack of smallpox; such results as he observed are quite in consonance with those obtained at the present day. One attack of smallpox will, in the vast majority of instances, protect against a second attack of the disease. Inasmuch, however, as complete immunity is not invariably conferred against smallpox, it is not to be expected that a permanent insusceptibility to cowpox will be produced. Therefore it is quite possible to successfully vaccinate a certain proportion of persons who have some years before passed through an attack of variola. But, in our experience, it is not possible to produce a successful vaccine lesion in an individual who has but recently been the subject of smallpox. We have repeatedly tried to vaccinate persons who have recently recovered from smallpox, but always without success, even in individuals who had never been vaccinated.

RETROVACCINATION OR VACCINATION FROM THE HUMAN SUBJECT BACK TO THE BOVINE SPECIES.

The inoculation of lymph from a human vaccination into the cow produces quite constantly a typical vaccine lesion. This expedient was at one time resorted to with the view of restoring potency to the attenuated lymph of long humanization. Most careful investigators concluded, however, that long humanized virus so transplanted gained neither in strength nor in purity, and, indeed, became more difficult to retransfer back to the human subject, although this difficulty was overcome in the second human remove. Retrovaccination is seldom employed at the present day.

VACCINAL SCARS.

Physicians are often in doubt as to what constitutes a typical vaccine cicatrix. We deem the subject of sufficient importance to warrant a brief study of the objective features of vaccination scars.

When an individual has undergone a vaccinia which has been perfect in every respect, there is left after the fall of the crust a cicatrix which is characteristically distinctive in its features. Such a scar is indicative of the fact that the bearer thereof has passed through the vaccine disease in its most perfect form. The typical cicatrix is round or oval, distinctly excavated, with well-defined margins, reticulated or foveolated, and altogether presenting the appearance of having been stamped into the skin with a sharply cut die. Not all true vaccinations are followed by scars presenting these characteristics, but the more closely the cicatrix approaches to this standard the greater is the assurance that the vaccine disease has been genuine in every respect, and is calculated to give the greatest degree of immunity against smallpox. However, the appearance of the scar may vary within certain limitations and still be regarded as the sequential imprint of a genuine vaccinia.

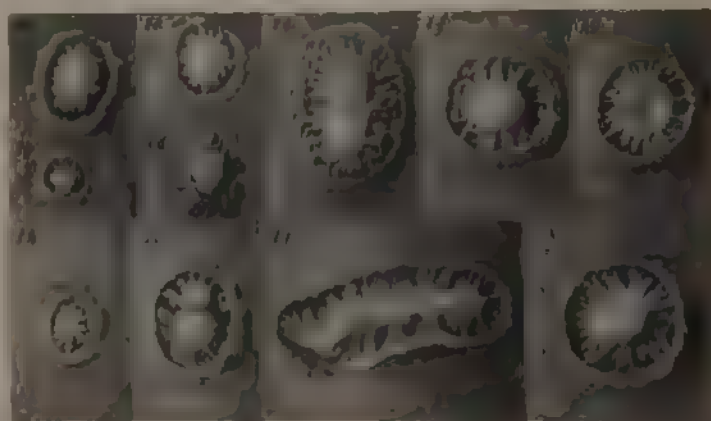
The variety of vaccine scars is very great; the most frequent variations from the type above depicted are the result of the employment of lymph which has become more or less enfeebled by long human transmission. Modifications of the resulting scar may also be due to abnormalities or complications of the vaccine process, and to mechanical injury or interference with the normal development of the vesicle.

In 1851, Decanteleu, of Paris, published an excellent monograph on the subject of vaccine scars, in which the classification is given after the system of Lamarck.¹ The author distinguishes fifteen species of vaccine scars and depicts these and many subvarieties in well-executed drawings, some of which are here reproduced. These drawings represent the type of each species. Fig. 10 represents examples of perfect scars resulting from vaccinations with vigorous bovine lymph or of an early

¹ *Monographie des cicatrices de la vaccine*, par J. E. B. Denarp-Decanteleu, Paris, 1851. Quoted by Dr. H. A. Martin.

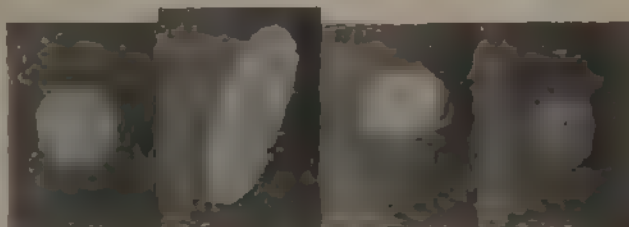
human remove therefrom. The centre of the cicatrix is rounded, smooth, and convex, and surrounded by a deep, depressed, circular furrow or sulcus, which is traversed by short ridges radiating from the centre to the periphery. Most of these scars are round, but occasionally those of oval shape are encountered. Decanteleu found this type of scar in 24 per cent. of over five thousand scars examined.

FIG. 10



Various forms of good vaccine scars, showing a central, elevated disk surrounded by a furrow with radiating bands, the scars look as if they had been punched out with a die. (After Denarp-Decanteleu)

FIG. 11



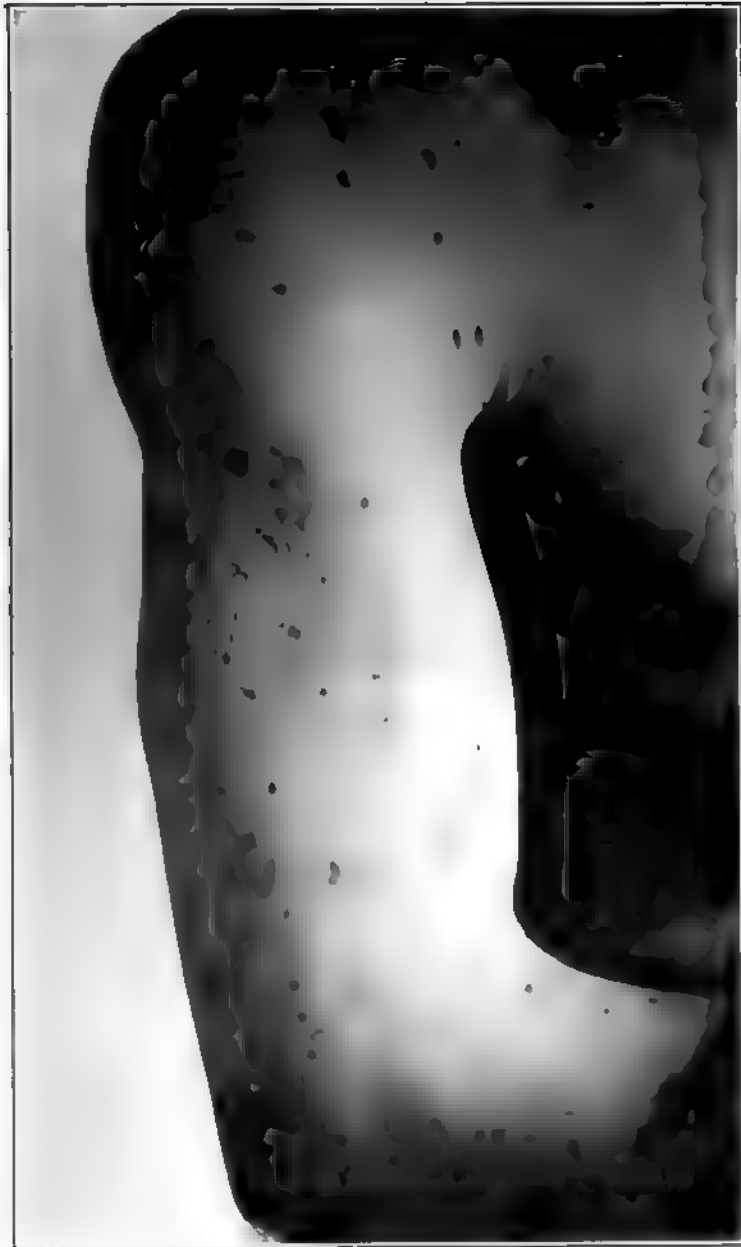
Smooth scars or a pimple, with the surrounding skin showing slight pitting, such scars may result from genuine vaccination with living humanized virus. (After Denarp-Decanteleu)

It is but natural that vaccine scars should present variations. A cutaneous scar, no matter from what cause, is the result of the destruction of dermal tissue. When merely epidermis is lost no scar results, for the cells of the *rête mucosum* proliferate and restore the complete integrity of the cuticle. When, however, a portion of the cutis proper is destroyed, repair takes place through the formation of fibrous connective tissue, which is scar tissue.

The appearance of a cicatrix will depend upon the character, extent, and depth of the tissue loss, and sometimes upon certain personal predispositions.

The minute *foveolations* or *pits* which are commonly seen in vaccine

PLATE II.



Four Good Scars from an Infantile Vaccination.

Scars show pitting and depression beneath surrounding skin. Patient contracted in adult life a mild, modified smallpox for which he was treated at the Municipal Hospital. Stains of smallpox lesions visible in photograph.

scars, and which are regarded by some as essential to the perfect cicatrix, represent the dilated orifices of hair follicles and sebaceous glands. It is readily seen that if the vaccine process destroys the skin to a sufficient depth the hair follicles and glands may be obliterated and the resultant scar may be devoid of the pits referred to. It is not at all rare to see scars from burns, ecthyma, and perhaps also furuncles, which, owing to the presence of numerous pittings, present an appearance which closely simulates vaccine cicatrices.

The peculiar foveations or large, excavated pits seen in the peripheral portion of a vaccine scar probably result from the specific histological changes in the vaccine vesicle, each excavation doubtless representing the floor of a dissepiment or cellular compartment.

The greater the vigor and activity of vaccine lymph, the more inflammatory is the process and the deeper is the tissue destruction. Animal lymph, which is more vigorous than virus of long humanization, produces a larger and deeper-seated vaccine lesion and consequently a larger and more pronounced scar. The cicatrix following the use of long humanized virus is often quite small and but little depressed beneath the level of the skin. The depth of involvement of the true skin appears to be inversely proportionate to the number of human removes from the original cowpox source.

Size of Vaccine Scars.—Of 3493 round scars examined by Decanteleu, 2758, or about 75 per cent., had a diameter of 6 to 9 mm. Sixty-three measured 4 mm., eleven measured 20 mm., while the remainder had intermediate dimensions.

With the animal lymph now in use the average diameter of the scar is certainly greater than those studied by Decanteleu. It is not rare to observe scars measuring half an inch (12 mm.), three-quarters of an inch (18 mm.), and even one inch (24 mm.), and scars below one-third of an inch (8 mm.) are uncommon.

We occasionally encounter much larger scars which are smooth and glossy and devoid of foveations, which have evidently resulted from sloughing of the skin. While it is quite possible that the vaccine process in such cases has conferred protection, it is impossible, owing to the absence of the characteristic features of the scar, to be sure that such is the case. A large scar, therefore, does not necessarily mean a good scar.

In some individuals, particularly negroes, scar tissue tends to become hypertrophic and keloidal in character. It is not uncommon in the dark race to see the vaccinal scar smooth and elevated like a button, instead of being excavated or depressed. This change does not interfere with the protection which the vaccination confers, but does obscure to some extent the true estimate of the perfection of the antecedent vaccine disease.

Upon spontaneous detachment of the vaccine crust the underlying scar tissue is seen to be quite reddened. This is, of course, due to the hyperæmia or excessive amount of blood in the skin. In the course of some months the color fades away and the scar tissue becomes whiter

than the surrounding skin. While the redness persists the scarring is not so easily perceived; later it becomes more visible.

In the course of many years, however, the vaccine scar often loses some of its distinctness and becomes less conspicuous. Indeed, where the original scar has not been pronounced, it is possible for it to fade to such an extent that after a lapse of many years it may no longer be visible, but disappearance of the scar is not likely to result where the original vaccinia has been perfect in every respect.

Scars After Revaccination.—The degree of perfection of a revaccination depends, as has been previously stated, on the extent of vaccinal susceptibility remaining in the individual. The more nearly the secondary vaccination resembles a primary vaccinia, the more closely will the cicatrix conform to the standard described above. Revaccinations are, in the vast majority of instances, considerably modified. They produce what has been aptly termed vaccinoid. This modified process is usually followed by a scar which commonly presents upon its surface minute pittings. Where but little vaccinal susceptibility remains, and the process is greatly modified, it is quite possible that no indelible scar will be left. Usually, however, a pitted scar marks the site of a successful revaccination.

Discolorations are not infrequently seen after unsuccessful attempts at vaccination or revaccination. These are sometimes of a brownish color, representing an increased deposit of pigment; at other times the pigment is lost, leaving a white spot which is neither elevated nor depressed. Occasionally the lines of scarification produced by a pointed instrument will remain visible for a long time, although the vaccination has been unsuccessful.

Prognostic Import of Vaccine Scars.—It has been clearly shown that the degree of vaccinal protection is proportionate to the perfect evolution of the vaccinia. Marson and others of large experience have found that smallpox is less fatal among patients who bear unmistakable evidence, in the form of typical scars, that the vaccine disease has run a perfect course. While Jenner never said very much about the character of the scar, he nevertheless constantly insisted that the vaccinal process should observe a certain definite course in order that the protection should be perfect.

In examining the vaccine cicatrices of a large number of persons, it is found that the scars differ considerably in appearance and degree of perfection; the question arises, Can protection be measured to any degree by the different characteristics of the scars? There is no doubt that many persons with quite inferior vaccine marks are fairly well protected, or even enjoy immunity against smallpox, while some with typical marks prove to be susceptible to the disease, and indeed sometimes perish from it. But such results must be regarded as exceptions to the rule. When a large number of patients are examined and the results tabulated, the degree of protection is found to bear a very close and direct relation to the character of the vaccine cicatrices.

All of the patients represented in the subjoined tables were carefully

examined on their admission to the hospital, and the number and character of their vaccine scars at once recorded. At this time it was, of course, impossible to foretell the final outcome of the disease. The scars are divided, according to their quality, into three grades, which are designated in the tables by the terms *good*, *fair*, and *poor*. Under the first head are included all cases presenting typical vaccine cicatrices—that is to say, cicatrices which are distinctly excavated, with well-defined margins, reticulated or foveolated, and altogether presenting the appearance of having been stamped into the skin by a sharply cut die. Under the second head are included all cases with scars having the same general characteristics, though much less distinctly marked. Under the third head have been classified all cases having scars which were said to have been the result of vaccination, but which in very many instances were so indistinct or uncharacteristic as to make it difficult and sometimes impossible to recognize them as vaccine scars.

In the cases classified under the heads of both *good* and *fair* marks the patients had all, doubtless, passed through a well-marked or reasonably well-marked course of vaccinia in infancy. We are strongly of the opinion that very many of the cases classified under the head of “poor cicatrices” were never successfully vaccinated. Very often we felt fully convinced at the time of making the examination and recording the vaccine condition that such was the case, but, as the patients insisted that they had been vaccinated, we could not reject their testimony without being considered, especially by the enemies of vaccination, partial judges. It certainly does not detract from the reputation of vaccination to know that when the vaccine process is irregular, imperfect, or spurious, the protection is diminished or absent. As the mean death rate of the cases showing *good* and *fair* cicatrices is 8.34, and the death rate of those showing poor scars is 22.64, it is evident that not only very many of the latter had been imperfectly vaccinated, but that a large number had never been subjected at all to the vaccine influence.

As tending to show that the degree of protection can be measured to a considerable extent by the quality of the vaccine scars borne by persons, the following table of cases of smallpox treated at the Municipal Hospital is presented:

	Cases.	Deaths.	Percentages of deaths.
Vaccinated in infancy, good scars	2335	152	6.5
“ “ “ fair “	1105	135	12.21
“ “ “ poor “	1524	345	22.64
Postvaccinal cases	4964	632	12.53
Unvaccinated “	3687	1542	41.82
Total	8651	2174	25.13

The opinion has been advanced, more especially by Marson and other English writers, that the degree of vaccinal protection in an individual is directly proportionate to the number of insertions made.

Marson based this opinion upon an extended experience with smallpox, in which he found that the disease was less severe and less fatal in proportion to the number of vaccine scars that the patient presented.

The following table published by Marson gives an analysis of all the cases of smallpox admitted into the London Smallpox Hospital between the years 1836 and 1855:

Patients admitted with smallpox.	Number of patients.	Character of scar.	Cases.	Died.	Rate % of mortality from smallpox after deducting deaths from superadded diseases.
1. Having one vaccine scar . .	2001	{ Good Indifferent	1032 969	54 134	3.83 } 7.73 11.91
2. Having two vaccine scars . .	1446	{ Good Indifferent	873 573	32 57	2.32 } 4.70 8.34
3. Having three vaccine scars . .	518	{ Good Indifferent	307 211	7 9	0.99 } 1.95 3.84
4. Having four or more vaccine scars.	544	{ Good Indifferent	358 186	2 3	0.55 } 0.55 0.54
5. Stated to have been vaccinated, but having no scar.	370	370	101	23.57
6. Stated to have been vaccinated, but particulars of cicatrix not noted.	17	17	3	6.66
Total	4896	402	6.56

In addition to Marson’s statistics the English Vaccination Commission presents observations on 6839 other cases. The figures are as follows:

Scars.	Cases.	Deaths.	Percentages.
1 scar	1357	85	6.2
2 scars	1971	115	5.8
3 scars	1997	75	3.7
4 scars	1514	34	2.2

In summing up, the Commission says: “The evidence appears to point to the conclusion that the greater the number of marks the greater is the protection enjoyed by the vaccinated person in relation to smallpox. This further indication also seems to be afforded, that while the duration in this respect between those with one and those with two marks is not very great, there is a very marked contrast between those with four or even with three marks as compared with those with either one or two.”

Our own experience on the comparative protection conferred by multiple scars does not entirely coincide with that of the English writers, as will be seen on reference to the following table:

**CASES OF SMALLPOX TREATED IN THE PHILADELPHIA MUNICIPAL HOSPITAL
FROM 1871 TO 1903, INCLUSIVE.**

Number of vaccine scars and death rate.

	Cases.	Deaths.	Percentages of deaths.
Unvaccinated	3220	1392	43.23
Claiming to have been vaccinated; no visible scar	258	150	58.13
Vaccinated seven days or less before variolous eruption	106	39	38.79
" longer than seven days before variolous eruption	264	39	14.77
Vaccinated in infancy, one good scar	1282	84	6.55
" " " " fair " " " " " " " " " "	695	90	14.39
" " " " poor " " " " " " " " " "	1176	293	24.83
Total number showing one scar	3153	467	14.81
Vaccinated in infancy, two good scars	486	28	5.76
" " " " fair " " " " " " " " " "	182	19	10.44
" " " " poor " " " " " " " " " "	153	30	19.61
Total number showing two scars	821	77	9.50
Vaccinated in infancy, three good scars	183	11	6.01
" " " " fair " " " " " " " " " "	65	4	6.15
" " " " poor " " " " " " " " " "	72	14	19.44
Total number showing three scars	320	29	9.06
Vaccinated in infancy, four or more good scars	291	25	8.58
" " " " " " fair " " " " " " " " " "	95	11	11.57
" " " " " " poor " " " " " " " " " "	105	12	11.42
Total number showing four or more scars	491	48	9.77

We believe that the *quality* of vaccine scars is a far more reliable index of the degree of protection than the *quantity*. The table shows that when the scars are typical it makes but little difference whether they are single or multiple, the protection being almost the same. There is no doubt that vaccinia characterized by a single typical vesicle confers immunity against smallpox; it is impossible for multiple vesicles to do more. We have seen some adults with smallpox who bore upon their arms as many as twenty scars from an infantile vaccination; they appeared to be no better protected than individuals with one scar of equal quality.

We have seen a girl of twelve years who had six vaccination scars from infancy contract smallpox; the six insertions did not seem to confer greater protection than one ordinarily does.

However, as a safeguard against failure when the danger of variolous infection is imminent, it is advisable in vaccinating to make more than one insertion.

The English Vaccine Commission report indicates that patients with foveated scars enjoy an advantage, both as far as the fatality and the mildness of the disease are concerned, over those with unfoveated scars. The data upon which this conclusion is based are, however, too limited to warrant any too great importance being laid upon this point. Furthermore, in the statistics of some outbreaks the figures were by no means conclusively in favor of the foveated class.

There was some evidence to support the view that there was superior protection according as the area of the vaccination marks was larger.

VACCINAL COMPLICATIONS AND INJURIES.

The chapter on vaccination statistics will indicate the great life-saving power of vaccination. During the past century there have been probably more than fifty million human lives preserved through its beneficent influence. If accidents have now and then attended the practice of vaccination and deaths have resulted therefrom, deplorable though these results may be, they fade into insignificance when compared with the inestimable benefits conferred by this procedure.

In discussing the complications and accidents of vaccination we have tried to preserve a fair judicial attitude. We present the entire list of injuries that have been claimed from time to time to result from vaccination. The list is a long and formidable one and calculated to convey the impression to the mind of the inexperienced that vaccination is a dangerous procedure. We desire to point out the fact that many of the enumerated conditions are excessively rare, and that others are not the result of vaccination at all, but are inserted in order to be fairly discussed.

Vaccinal Mortality.—The practice of vaccination is a measure which is not absolutely unattended with risk. It must be remembered that vaccinia is an infectious disease, and that some danger attaches to the mildest diseases of this character. Furthermore, vaccinia is complicated by the presence of a wound, and cutaneous wounds, particularly if neglected, are liable to infection with disease-producing germs. Even a pin scratch has on more than one occasion given opportunity for an infection which has resulted in death.

Most of the injuries and fatalities that from time to time result from vaccination are preventable. Already the use of bovine lymph, special methods of preparation and preservation, an improved vaccination technique, and care of the vaccinated arm have taught us how to avoid most of the vaccinal complications.

Deaths have from time to time resulted from vaccination, but the number is exceedingly small when compared with the enormous number of vaccinations performed.

In England, where antivaccination prejudice is strongest, the alleged death rate is the highest. According to the Registrar General's return from 1881 to 1889 the number of deaths certified as connected with vaccination was 476, or about 53 a year. Inasmuch as 6,739,902 primary vaccinations were performed during this period of nine years, we have an average death rate of 1 to 14,159 primary vaccinations. Admitting that vaccination was really accountable for all of these deaths, the mortality rate is, as Acland has pointed out, still far below that attendant upon the use of chloroform as an anæsthetic.¹

¹ The deaths from chloroform in England are about 1 in every 2000 anæsthesias; from ether, 1 in 20,000.

The mortality of vaccination in Germany carefully estimated by Voigt¹ is stated to have been 35 in 2,275,000 vaccinations (a ratio of 1 death to 65,000 vaccinations), including both primary and secondary insertions. Of the deaths, 19 were due to erysipelas, 8 to gangrene, 2 to cellulitis, 3 to "blood poisoning," and 3 to other causes.

Voigt himself during an experience of twenty years vaccinated over a quarter of million of people. Within the last five years he has vaccinated 100,000 people with but a single death. This is an evidence of the results that may be expected when all precautions are taken.

Kübler² states that in the thirteen years from 1885 to 1897 there were recorded 113 deaths among 32,000,000 vaccinations in the German Empire; 46 of these deaths were shown to have been caused by subsequent wound infection through some neglect on the part of the patient. In only 67 cases was there a connection with the vaccination itself; even in these cases the relation was not proved, but it could not be disproved. Admitting that all of the 113 deaths resulted from vaccination, this would give a rate of 1 death in every 283,177 vaccinations.

When this mortality is compared with the hideous loss of life from smallpox in the prevaccination days, and when it is recognized that properly repeated vaccination is an absolute safeguard against smallpox, the virtues of this procedure can be properly appreciated.

It is a judicial weakness of human judgment to confound sequence and consequence; and the medical mind even in matters medical is not exempt from this failing. It is scarcely to be wondered at, therefore, that laymen with but a hazy comprehension of medical theory and practice should view a succession of events in the light of cause and effect. It would be a difficult matter to prove to the average individual that a cutaneous disease appearing within a few days after the performance of a vaccination was not the result of it.

Vaccination is more universally practised throughout the entire world than any other medical procedure. Probably three-quarters of all civilized people submit to the inoculation of vaccine material in order to be granted immunity against smallpox. In Germany alone, from 1885 to 1897, 32,000,000 people were vaccinated.

In the natural course of events it must occur that among millions of people there will be some in whom the vaccination will have just preceded the development of some disease or other. Laymen and even physicians are too prone under such circumstances to apply the principle of *post hoc ergo propter hoc*. Vaccination immunizes only against smallpox; it will not protect one from tuberculosis, syphilis, skin diseases, etc. Therefore, as these are common diseases, it will of necessity happen that they will from time to time attack persons who have been recently vaccinated. We do not desire to convey the impression that vaccination never does any harm, but we are convinced that many morbid conditions are attributed to vaccination which bear no relation to it save a chronological one.

¹ Quoted by Holt, Diseases of Children.

² History of Smallpox and Vaccination, 1901.

Vaccination and Cutaneous Disease.—The following classification of skin diseases associated with vaccination is a modification of that formulated by Malcolm Morris and later revised by Frank:

I. Eruptions attributable to the vaccine virus pure and simple.	Local	{ Normal vaccinia. Erythematous dermatitis (areola).
	Constitutional	{ Generalized vaccinia. Diffuse vaccine erythema. Vaccinal roseola. Vaccinal lichen. Vaccinal miliaria. Purpura. Erythema multiforme. Urticaria.
II. Eruptions attributable to mixed infection at time of vaccination or later.	Local	{ Erysipelas. Impetigo contagiosa. Furunculosis. Vaccinal ulcer. Localized gangrene. Cellulitis.
	Constitutional	{ Disseminated gangrene. Syphilis. Leprosy (?). Tuberculosis (?).
III. Eruptions sometimes following vaccination.		{ Eczema. Bullous eruptions (acute pemphigus, dermatitis bullosa, dermatitis herpetiformis). Psoriasis. Furunculosis. Urticaria.

The above classification is doubtless faulty in many respects and open to criticism, but will perhaps serve the purpose of indicating in a general way the etiological factors in the production of the various dermatoses that may complicate vaccinia.

Generalized Vaccinia.—This is perhaps the only eruption among those enumerated (with the exception, of course, of the normal vaccine disease) which may with positiveness be attributed to the pure vaccine virus. There are two varieties of generalized vaccinia—1. Spontaneous generalized vaccinia (vaccinal eruptive fever, vaccinola). 2. Generalized vaccinia from autoinoculation.

Spontaneous generalized vaccinia is an extremely rare condition; many cases formerly regarded as instances of spontaneous diffusion of the eruption are in all likelihood cases of autoinoculated vaccinia. The eruption appears usually from the fourth to the tenth day after vaccination and most often from the sixth to the ninth day.

The lesions appear in successive crops and pass through the stages of papule, vesicle, and pustule. The eruptive lesions, being of different age, may be seen in varying stages of development. Complete subsidence of the efflorescence usually occurs before the twenty-first day. The lesions may be few or numerous and may appear upon any portion of the body surface. Fever is absent in some cases and present in others, being usually proportionate to the extent of the eruption and the associated complications, particularly glandular enlargement.

The causes of generalized vaccinia are but poorly understood. An abnormal susceptibility to the vaccine virus has been invoked as a cause. The administration of the vaccine material through the digestive, circulatory, or respiratory system is regarded by Acland as capable of

inducing a generalization of the eruption. This writer mentions an observation of Etienne that a generalized vaccinal eruption had been produced in children who had sucked their vaccination pocks; generalized vaccinia has also been produced by the intentional feeding of powdered vaccine crusts to subjects previously regarded as insusceptible to vaccinia.

Chauveau was able to produce a generalized eruption in horses by subcutaneous injection of vaccine lymph and also by administration through the respiratory and digestive tracts.

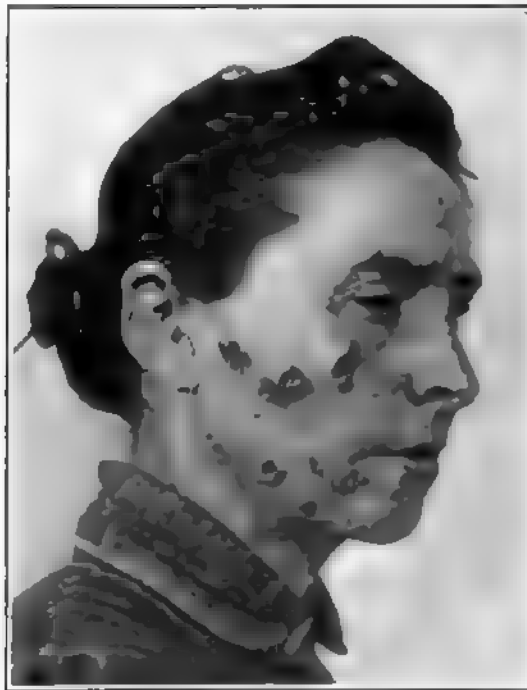
Generalized vaccinia may present a considerable resemblance to variola. It may usually be distinguished by the absence of an initial stage, its occurrence after vaccination, the appearance of the eruption in crops, and the irregular distribution of the lesions. Its differentiation from inoculated variola is rather more difficult.

Generalized Vaccinia from Autoinoculation.—This form of generalization of the vaccine lesions is by no means rare. Many writers at the present day are inclined to regard the vast majority of cases of generalized vaccinia as due to external inoculation. French writers have reported a number of instances of diffusion of the vaccinal eruption over an extensive cutaneous area the seat of a moist eczema. Unless there is danger of exposure to smallpox, it is, indeed, advisable to postpone vaccination if the subject is suffering from a dermatosis in which there is denudation of the skin. The number of lesions may be but two or three or there may be a profuse eruption. The development of a few supernumerary lesions in the neighborhood of the original vaccine insertion is by no means uncommon; this may occur even when there is no demonstrable abrasion of the skin. The virus may be transferred by the patient himself through scratching, or it may be conveyed by a second person. Fig. 12 represents six vaccine lesions upon the face of a woman which were produced by the finger-nails of an infant in arms; both the mother and child had been vaccinated upon the arm. We recall the case of an infant born of a variolous mother at seven and a half months. The child was immediately vaccinated, the insertions "taking" well. From eleven to fourteen days after the vaccination, lesions indistinguishable from vaccine vesicles appeared upon the left side of the thigh, the left loin, the middle of the back, the hip, the splenic region, and the scrotum. These varied in diameter from five-eighths of an inch to three-quarters of an inch, were depressed in the centre, the depression later acquiring brownish crusts. Sixteen days after the vaccination a half-dozen firm variolous papules developed upon the face, neck, scalp, and foot. The infant was feeble and died a few days later. In this case it was difficult to determine whether the multiplicity of vaccine lesions was due to circulatory diffusion or autoinoculation. Accidental vaccine lesions may appear upon any portion of the cutaneous or mucous surfaces. They may even occur upon the conjunctiva or upon the eyeball. In the latter case there may be loss of vision. One of the writers recently saw in the practice of a medical friend, an ophthalmologist, a case in which a vaccine lesion

had been accidentally produced upon the bulbar conjunctiva. The family physician while vaccinating several children was requested by the mother to remove a foreign body from her eye. The physician, without cleansing his hands, everted the eyelids to determine the presence of the offending substance. In the due course of time a vaccine vesicle appeared, accompanied by tremendous chemosis; the eye was saved only after prolonged skilful treatment.

The lesions in vaccinia generalized by autoinoculation appear at intervals after the original vesicle is well advanced; they seldom continue to make their appearance after the third week.

FIG 12



Accidental, multiple vaccinations produced by the scratching of an infant's hand contaminated from a vaccine lesion on its own arm.

Sore Arm.—Under this caption we shall discuss a condition which only in its severer phases is to be regarded as a complication. A certain amount of inflammatory reaction (areola) about the fully developed vesicle is to be viewed as a not undesirable and probably an essential part of the normal evolution of the vaccine lesion. It not infrequently happens that instead of a moderate erythema and oedema of the skin, these phenomena are present to an excessive degree. Now and then the inflammation about a vaccination reaches a violent degree of intensity and spreads over a considerable portion or the whole of the affected arm. In such cases the cellular tissue may become implicated, giving

rise to a diffuse *cellulitis*. The arm under such conditions is red, swollen, hot, and painful, and there is apt to be some associated systemic disturbance.

In other cases the inflammation is more circumscribed and its force is spent upon the vaccine lesion and the skin in its immediate neighborhood. In such cases a necrosis of the cutaneous and subcutaneous tissues may occur, with the formation of a slough. When this is thrown off an ulcer is left at the site of vaccination. In other cases the vaccinia may pursue a normal course to the development and decline of the areola, but instead of the formation of a typical scab an excavated ulcer appears, covered by a soft, thin crust, which frequently falls off and is renewed. the ulcer persisting in this manner for a long time. Mar-

FIG. 13



Sloughing at the vaccination site accompanying an unusually inflammatory vaccination.

tin, of Boston, repeatedly observed this irregular course upon arms which had been vaccinated with long humanized virus, whereas upon the opposite arm on which bovine virus had been simultaneously employed a perfect result was obtained.

This observation, as well as the scientific investigations of later-day observers, suggests that the excessively "sore arm" is due to the introduction of something in addition to the pure vaccine virus, and, furthermore, that this additional something is of the nature of extraneous micro-organisms. The *Lancet* Special Commission on Glycerinated Lymph¹ says that "the presence of a large number of organisms in an

¹ London *Lancet*, 1902

active vaccine lymph renders the local lesion more severe," and that "many of the bad results obtained in vaccination are due to imperfect sterilization of the skin and want of protection against the invasion of the weakened and abraded tissues by extraneous organisms." It is also stated that "one of the most certain methods of producing severe œdema is for the patient to use his arm freely and to bring about perspiration just before and after the vesicles have begun to form."

It is not uncommon for the arm to become very "sore" as the result of thoughtless or accidental traumatism on the part of the vaccinée. The vesicle is frequently ruptured by a blow, friction of clothing, scratching, and other like causes. Where the vesicle is unprotected the shirt-sleeve often becomes glued to the vaccination lesion, and attempts at separation cause a detachment of the crust. All of these forms of traumatism doubtless act in the same manner; they prevent the formation of a firm, compact crust which is nature's protective covering of the vaccine wound. By opening up the wound they permit of infection with extraneous germs which may produce merely excessive inflammation or may lead to ulceration or other more severe vaccinal complications.

Inasmuch as we can obtain a lymph which is rendered free of extraneous germs by the process of glycerinization, by proper care of the arm before, during, and after vaccination, we should be able, in the vast majority of instances, to prevent the development of "sore arms."

Vaccinia Hemorrhagica.—From time to time cases of vaccinia are seen in which the areola about the vesicle at the acme of its development becomes hemorrhagic, assuming the appearance of a diffuse ecchymosis. In some instances the skin beyond the areola may present a bluish appearance. In rare cases there may occur scattered petechiæ and ecchymosis and hemorrhages from some of the mucous membranes. The cause of this complication is obscure; it is doubtless not so much due to any peculiarity of the lymph as to some underlying systemic condition favoring hemorrhagic extravasation, such as scorbutus.

Vaccinal Ulceration.—Ulceration at the site of insertion of the lymph is by no means an uncommon complication of vaccinia. Acland¹ says that nearly 4 per cent. of the vaccinal injuries inquired into by the English Local Government Board (1888-91) were due either to ulceration or glandular abscess. There is in all probability one of two factors which may give rise to vaccinal ulceration—either the introduction into the skin of extraneous micro-organisms (at the time of vaccination or later) capable of producing a tissue necrosis, or an abnormal or vitiated state of health which permits of an excessive and unusual local reaction. Both of these factors appeared to play an important role in the production of "bad arms" among the soldiers during the United States Civil War. In the admirable report of the Board of Health of Louisiana of 1884, compiled by Dr. Joseph Jones, we read the following: "In scorbutic patients all injuries tended to form ulcers of an unhealthy character, and the vaccine vesicles, even when they appeared at the proper time and manifested many of the usual symptoms of the vaccine disease,

¹ Article on Vaccinia, Allbutt's System of Medicine, p. 596.

were nevertheless larger and more slow in healing, and the scabs presented an enlarged, scaly, dark, unhealthy appearance. In many cases a large ulcer, covered with a thick, laminated crust, from one-quarter to one inch in diameter, followed the introduction of the vaccine matter into scorbutic patients." In the same report Dr. Paul F. Eve describes certain abnormal manifestations of the vaccine disease due to the use of an improper scab. "The scab used in Atlanta which did so much mischief was soft, porous, and spongy, resembling concrete inspissated pus. . . . In every instance in which vaccination was attempted with it, premature effects were developed. No proper period of incubation nor papular nor vesicular eruption was observed, but in a few days, even as early as the second, inflammation had set up, and by the fourth or fifth day sores were produced, covered by a thick, dirty crust, with an ichorous discharge. Soon an ill-constituted ulcer, with perpendicular edges, ensued, extending through the dermoid to the cellular and muscular tissues, and involving the neighboring lymphatics." These citations indicate that either a weakened resistance on the one hand, or an extraneous infection on the other, may be responsible for vaccinal ulcerations.

We have seen a few cases of ulceration at the vaccination sites following the use of bovine lymph. Fig. 13 shows such an ulceration occurring about the fifteenth day after vaccination.

Septicæmia and Pyæmia Following Vaccination.—Blood poisoning is a rare condition after vaccination at the present day, and with care in the propagation and preservation of lymph, an aseptic technique, and proper protection of the vaccinated arm, this unfortunate complication will doubtless become rarer still. Several appalling epidemics of septicæmia after vaccination are on record; one occurred in the United States, one in Germany, and one in France. In all three the disastrous results followed the use of humanized virus; in two instances there was the grossest negligence in the preservation and preparation of the crusts, and in the third a lymph was used which was producing in progressive transmissions increasingly abnormal reactions.

These epidemics are of much importance, and a brief account of them is herewith presented:

In 1860, during the prevalence of smallpox in Westford, Massachusetts, a physician vaccinated a number of people with crusts which had been shaken up in a bottle with snow-water in order to provide a sufficient quantity of vaccine material. For ten or eleven days patients were vaccinated with a lancet which was from time to time dipped into the bottle. None of these people showed any results; but on the eleventh or twelfth day, by which time the bottle of liquid emitted a horrible stench, he "vaccinated" twenty-five more people. There at once ensued in half the cases diffuse abscesses. Three of the oldest vaccinées died in a short time, and a dozen or more of the remainder were only saved by the most prompt and energetic treatment.¹ As Dr. Martin, who was foreman of the coroner's jury on this occasion, stated, "the

¹ Mentioned by Dr. Henry A. Martin. Reprint from a letter in the Erie Observer.

fearful results were clearly to be ascribed to the development of a septic poison of intense and virulent malignancy at a certain stage of the decomposition of animal matter."

In 1878, at Grabnick, a similar but more extensive epidemic of septicæmia occurred among children infected with some old virus which had been exposed to the air for a long time. Fifty-three children were inoculated with the decomposed vaccine material, and of this number fifteen died. Some of the children had morbilliform and scarlatiniform eruptions, and others abscesses and erysipelatous symptoms. According to Pincus the vaccine material contained septic bacteria. Autopsies were made upon two children and the deaths ascribed to septicæmia.

Brouardel¹ reports a series of cases of blood poisoning following vaccination at Asprières, France, in 1885. Brouardel, Pasteur, and Proust were commissioned to determine the responsibility of the attending physician. The commission says: "In our investigations we were enabled to trace the vaccine back through five generations and to determine that it was by employing a virus originally good, but which gave rise successively to accidents, at first of slight gravity, then more and more serious, that the preparation was made for the final disaster." Forty-two children were vaccinated from the arm of a little girl who herself had developed fever the first night after her vaccination, and whose vaccination "took" on the following day. Of this number four died within twenty hours and two others later. Almost all of those vaccinated were more or less ill. The symptoms were fever, vomiting, diarrhœa, and in the fatal cases convulsions. The fever appeared at the latest eighteen hours after vaccination; in those who recovered it lasted from two to four days. All the children developed on the first day an inflamed area about 1 cm. in diameter surrounding the point of inoculation. A serous or seropurulent discharge occurred from the first to the third day. In all of the children a local and generalized impetiginous eruption followed the inoculation.

These cases represent examples of acute intense septicæmia analogous to that resulting from bad dissection wounds. The septic microorganisms were doubtless increased in virulency by successive transmissions from one subject to another.

A case of *pyæmia*² after vaccination is recorded in the *Lancet*, 1884, vol. i. p. 857. A child, aged six months, vaccinated with two other children from the same source, showed on the ninth day appearances of successful vaccination with no unusual symptoms, but on the sixteenth day the sores were ulcerated and freely discharging pus. The child was also suffering from bronchitis. Death took place on the twenty-fifth day after vaccination. The autopsy revealed the presence of pus in the left ankle, right sternoclavicular joint, both temporomaxillary articulations, and in the bursa over the right olecranon. The lungs presented a number of hemorrhagic infarcts.

¹ Twentieth Century Practice of Medicine. Article on Vaccinia, p. 534.

² Mentioned by Poole, Vaccination Eruptions, Edinburgh, 1893, p. 118.

There was in the same house a man with an abscess of the foot, and occasionally the mother had washed some linen in the water which had been used for cleansing his foot. This fact, with the early normal development of the vaccine lesion, and the exemption of the other two children vaccinated, constitute strong presumptive evidence that the septic infection occurred subsequent to vaccination, probably through neglect on the part of the child's caretakers.

Glandular and Subcutaneous Abscess.—In most normal vaccinations enlargement and tenderness of the neighboring lymphatic glands are observed. Where there is an unusual degree of inflammation about the vaccine lesion or actual ulceration, the swollen glands not infrequently undergo suppuration. As has been already stated, glandular abscess and vaccinal ulceration comprised nearly 4 per cent. of vaccination injuries reported to the English Local Government Board from 1888 to 1891. Sinigar¹ reports four cases of abscess among 1160 vaccinations. One appeared on the twentieth day in the lower half of the posterior triangle of the neck, one between the pocks on the arm on the twenty-fourth day, one on the arm on the twenty-ninth day, and one in the axilla on the thirty-second day. These abscesses are seldom of serious portent, usually healing rapidly after incision and evacuation.

Localized Vaccinal Gangrene.—In extremely rare instances death of the tissues *en masse* at the site of vaccination may occur, producing a localized gangrene. It would seem that in these cases the gangrene is due to low vitality of the tissues rather than to any impurity of the lymph. In cases observed by Balzer, Wheaton, and Acland, the children were of syphilitic parentage. Hutchinson, however, saw three cases of vaccinal gangrene in children in whom no such cause could be invoked. The view that the condition of the tissues is the most important etiological factor in the production of this complication is corroborated by the experience of surgeons in the Confederate army during the United States Civil War. Dr. Joseph Jones² writes: "After careful inquiry we were led to the conclusion that these accidents were, in the case of Federal prisoners, referable wholly to the scorbutic condition of their blood and the crowded condition of the stockade and hospital. The smallest accidental injuries and abrasions of the surface, as from splinters or bites of insects, were in a number of instances followed by such extensive gangrene as to necessitate amputation. The gangrene following vaccination appeared to be due essentially to the same cause, and in the condition of blood of these patients would most probably have attacked any puncture made by a lancet, without any vaccine matter or any other extraneous material."

Vaccinia Gangrænosa.—As has been pointed out by Crocker and others, the term vaccinia gangrænosa is a misnomer, inasmuch as the affection recorded under this title occurs after varicella (varicella gangrænosa) and other discrete pustular eruptions. Disseminated necrosis of the skin which in rare instances follows vaccinia, varicella, and

¹ Lancet, 1902.

² Report of Louisiana Board of Health, 1883-84.

pustular dermatoses may occur independently of these diseases in apparently healthy infants; a better designation, therefore, for this condition is *dermatitis gangrænosa infantum*. The gangrenous changes in the skin may occur early or late. Stokes,¹ of Dublin, reports a case of so-called vaccinia gangrænosa developing forty-eight hours after vaccination. The vaccinal or varicellous pustules may be directly converted into blackish sloughs, which are thrown off and leave deep, excavated ulcers; or the gangrene may not set in until a week or two has elapsed, beginning as papulopustules which crust over, become surrounded by an areola, and then break down and ulcerate. High fever is often present. The cause of this rare condition is obscure; it usually supervenes in the course of some pustular febrile disease,² particularly in tuberculous, syphilitic, or rachitic children. It is quite possible that the gangrene is due to infection with some virulent micro-organism.

Vaccinal Roseola (*roseola vaccinosa*, *vaccinal rash*, or *erythema*).—Under the above designations has been described a rosy, macular rash, which occasionally appears in vaccinated persons about the time of maturation of the vesicle. While this eruption is ordinarily seen about the tenth day after vaccination, it has been observed as early as the third day and as late as the eighteenth. It usually appears first upon the vaccinated arm, rapidly spreading to the trunk and other portions of the body. The macules are large, irregular, blotchy in appearance, of a rosy tint, and not elevated above the level of the skin. In rare instances the macules may coalesce, giving rise to a *diffuse erythema*. The eruption is of brief duration, lasting from a few hours to a day or two. It may be accompanied by moderate elevation of temperature.

The rash is not unlike that of measles, with which, indeed, it has not infrequently been confounded. The eruption of measles is more elevated, being maculopapular in character and more persistent, and is accompanied by higher fever and the characteristic catarrhal symptoms of this disease.

During epidemics of smallpox, vaccinal roseola has been mistaken for the beginning eruption of confluent smallpox. *Roseola vaccinosa* has a complete analogue in the *roseola variolosa*, an exanthem presenting almost identical features, which is not infrequently observed just before the appearance of the eruption of modified smallpox.

Vaccinal Lichen.—Crocker states that in his experience vaccine lichen has been the most common of the true vaccinal exanthema. He has made notes of twenty cases of this eruption. He states that it may be either papular, papulovesicular or pustular. It appears from the fourth to the eighteenth day, most commonly on the eighth; in about one-half the cases it is seen first on the arms, appearing in the remainder on the trunk, neck, or face; the eruption then extends in successive crops over large portions or the entire cutaneous surface (Fig. 14).

¹ Dublin Journal of Medical Science, June, 1880. Quoted by Crocker.

² The writers recall the case of a young girl suffering from smallpox, who developed at the end of the third week numerous punched-out areas of cutaneous gangrene. The patient succumbed to this complication, which was doubtless a condition analogous to the so-called vaccinia gangrænosa.

PLATE III.



Roseola Vaccinosa Appearing upon the Tenth Day
after Vaccination.

The papules are reddish, conical, pinhead sized, surrounded by a reddish halo, and often surmounted by minute vesicles or pustules. In the experience of the writers vaccine lichen has been excessively rare.

FIG. 14



Vaccination upon the tenth day, showing an unusually intense areola. A papular vaccinal eruption is also seen upon the face

Vaccinal Miliaria.—In rare cases instead of a papular eruption a vesicular outbreak may take place, usually from the eighth to the eleventh day. Danchez¹ writes: "We give the name vaccinal miliaria to a satellite eruption of the vaccinal fever, appearing from the eighth to the twelfth day (very rarely later) after vaccination. It is constituted by small vesicles of the size of a grain of millet, accumulated in great numbers over large surfaces, containing a transparent liquid at first, then opaque, followed by slight furfuration, and never leaving cicatrices after it."

¹ Vaccinides, Thèse de Paris, 1883.

A miliary vesicular eruption is occasionally seen in or around the vaccination areola. These vesicles are not true vaccine lesions, for Martin has shown that the contents inoculated upon another individual fails to produce the vaccine disease.

Erythema Multiforme and Urticaria after Vaccination.—The eruption of multiform erythema is occasionally seen in vaccinated individuals between the first and the tenth day after the insertion of the virus. In some cases the eruption is delayed considerably beyond this period. The lesions may be erythematous, papular, tuberculous, vesiculobullous or mixed.

At times the eruption is annular. Crocker saw a well-marked case which began on the ninth day after vaccination, and was characterized by shilling-sized annulopapular patches. Napier observed a case on the eleventh day which began as rings.

Not infrequently urticarial lesions are present, the eruption being a type of combined erythema multiforme and *urticaria*. Allen and Sobel regard urticaria as one of the most common of the generalized vaccinal eruptions.

Norman Walker¹ has observed five cases of erythema multiforme after vaccinations with glycerinated lymph. In all, the early course of the vaccination was uneventful. The eruption was invariably seen on the hands and face, but on other parts as well.

In a review of the vaccinal complications in 1160 vaccinations, Sinigar² states that there were 23 cases of erythema, including simple erythematous blushes, finely punctate erythemata, erythema of papular or urticarial type, and erythema multiforme. Concerning the date of appearance, 1 rash appeared on the third day, 5 on the eighth, 2 on the ninth, 5 on the tenth, 4 on the eleventh, 1 on the twelfth, 4 on the thirteenth, and 1 on the sixteenth day. No age was exempted; in 4 cases the patient was over seventy years of age. The average duration of the rash was forty-eight hours, but in 1 severe case it lasted six days.

Impetigo Contagiosa.—This contagious disease of the skin is extremely common, independent of vaccination, among dirty and poorly nourished children. Any abrasion of the skin increases the liability to its development. Its occasional occurrence after vaccination, particularly among children in poor hygienic circumstances, is therefore scarcely to be marvelled at. The introduction of the infection of impetigo with the insertion of the vaccine virus must be an occurrence of the greatest rarity; inasmuch as impetigo sores develop rapidly (from one to two days) after the skin is infected, we would expect, if the disease were invaccinated, to discover the impetigo lesions twenty-four to forty-eight hours after the vaccination.

As a matter of experience, however, impetigo usually develops at a considerably later period; it may make its appearance at any period up to the complete healing of the vaccinal wound. It is not infrequently observed at the end of the second or third week after vaccination. The

¹ British Medical Journal, 1901, p. 1201.

² Lancet, 1902.

first lesions are usually seen about the site of insertion of the vaccine lymph. This area may become quite inflamed, the surrounding epidermis raised up by a seropurulent fluid, and the process extend upon the periphery, with the production of voluminous ochre-colored crusts. From this as a focus other portions of the skin become infected by autoinoculation through scratching or other means. At times impetigo may assume a bullous form, simulating pemphigus; most of the pem-

FIG. 15



Secondary impetigo engrafted upon a late vaccination and subsequently upon other regions.

phigoid eruptions after vaccination would appear, however, to belong to the group of bullous dermatitis presently to be described.¹

In 1885 an outbreak of a cutaneous disease, said to have presented the clinical features of impetigo, occurred in villages on the Island of Rügen, in the Baltic Sea, after the vaccination of seventy-nine children.

¹ Engman and Grindon have each described (*Journal of Cutaneous and Genito-urinary Diseases*, 1901 pp. 140 and 188) extensive cases of bullous impetigo, not, however, related to vaccination. They state that this form of the disease is quite common in St. Louis, and that epidemics occasionally occur in foundling asylums, attacking particularly weak and undernourished infants. Some of the cases reported terminated fatally. [The differential diagnosis between bullous impetigo, acute pemphigus, and dermatitis herpetiformis is sometimes fraught with difficulty.]

Impetigo contagiosa is caused by invasion of the skin with the germs of contagious pus, independently of its source. There are probably two chief varieties due respectively to the streptococcus and the staphylococcus pyogenes.

Vaccinal Erysipelas.—Erysipelas is an acute infectious disease resulting from invasion of the body with the streptococcus of Fehleisen. In the vast majority of cases of this malady the infection gains its entrance to the system through a wound of the cutaneous or mucous surfaces; the disease therefore is essentially a wound infection.

Inasmuch as vaccinia is attended with the production of a wound of the skin, it is not surprising, particularly in view of the frequent neglect of vaccination wounds, that erysipelas should occasionally occur after this procedure. The erysipelatous infection is usually conveyed to the vaccination wound at some period subsequent to the insertion of the vaccine virus; in rare cases, however, the specific germs of erysipelas may be present in the lymph, in which event this complication develops on the second or third day after vaccination.

Erysipelas may develop in an infant after vaccination and still be independent thereof. Erysipelas is a common disease among infants; according to Dr. Ogle's testimony before the British Royal Vaccination Commission, two thousand per million infants under three months of age perish from it. It has been known to develop after very trivial injuries, such as the scratch of a pin, abrasion from the friction of clothing, etc.

Both vaccinal erysipelas and erysipelas from other causes are attended with a rather high mortality rate in infants. Of the deaths attributed to vaccination in England between 1886 and 1891 almost one-half resulted from erysipelas.

Erysipelas may result from the employment of lymph containing streptococci, from infected instruments, unclean hands, contact of soiled linen, or from previous contamination of the skin at the vaccination site. When the disease develops late it is often favored by injury or rupture of the vesicle, or forcible and premature detachment of the crust. Bad hygienic surroundings and uncleanness of the body or garments increase the liability to infection. Humanized lymph derived from a vaccinifer with an inflamed arm may give rise to erysipelas. The improper preservation of crusts has likewise given rise to some cases. One of the writers saw some years ago a series of cases of erysipelas follow vaccination with a humanized crust which had been rubbed up with water and kept in the pocket between two glass slides for several days, during which time decomposition had taken place.

As a vaccinal complication, erysipelas appears to be distinctly on the decrease. In 1877 Lotz was able to collect in Germany but two cases of death from this cause in 1,252,554 vaccinations.

The increased attention to asepsis in vaccination, the careful protection of the vesicle when formed, and the employment of bovine lymph will doubtless continue to lessen the frequency of this complication.

It is claimed that animal virus, on account of the comparative insus-

ceptibility of the bovine species to erysipelas, gives a greater security against this disease than humanized virus. In 1877 H. A. Martin emphasized this advantage of animal lymph in the most positive terms. He wrote: "During the sixteen years in which I supplied humanized virus the presence of this pest (erysipelas) in my practice and in that of my correspondents was the one great and serious drawback, the one formidable source of anxiety and blame. Since I have issued bovine virus to a far greater extent (from eight to nine thousand correspondents), I have never received a single complaint of the occurrence of erysipelas. It is said to attack particularly cases of revaccination, but in 1872-73 I revaccinated about twelve thousand patients with my own hand, and there was not one case of erysipelas among them all, nor have I ever known a case following the use of the bovine virus at any other time." Martin abandoned the collection and propagation of humanized virus in 1873 because in one week he had five cases of erysipelas. These children were vaccinated on one arm with the humanized lymph and on the other with the bovine product, and in each instance erysipelas appeared on the arm on which humanized virus had been employed.

True vaccinal erysipelas should be trenchantly distinguished from the dermatocellulitis which is not infrequently observed about the vaccine lesion, and which occasionally involves the entire upper arm and even the forearm; this is nothing more than an exaggeration of the inflammatory areola.¹ The arm is swollen and intensely reddened, but there is no tendency for the process to spread to other parts of the body, the inflammatory phenomena subsiding after the height of the vaccinia has been reached.

Tetanus Following Vaccination.—The development of lockjaw after vaccination was until a few years ago an occurrence of the greatest rarity. The minority contingent of the British Royal Vaccination Commission in 1896, after extended investigation, was able to mention but a single instance of this complication.

Tetanus after vaccination is said to be unknown in France, Germany, and other continental countries of Europe. Within the past five years (and particularly in 1901) a rather alarming number of cases has been reported in the United States. Dr. R. N. Willson and Dr. Joseph McFarland² have independently presented analytical studies of all of the cases recorded and of other cases personally communicated to them. Willson reports 52 cases and McFarland 95, 28 of which, however, are shrouded in considerable doubt.

Willson, from a painstaking study of the records of the cases reported, came to the conclusion that while the tetanus infection gained entrance at the site of vaccination, it was not introduced with the vaccine virus, but at some period subsequent to this.

¹ Some of the older writers, including Jenner, referred to this condition under the rather misleading designation of "erysipelatous inflammation;" but, as Jenner himself explains, it was not regarded as true erysipelas, but as merely bearing a resemblance to it.

² Proceedings of the Philadelphia County Medical Society, September, 1902.

McFarland, on the other hand, believes that tetanus organisms may be present in the virus, being derived from manure and hay; he further states that the future avoidance of the complication is to be sought for in greater care in the preparation of the virus.

In October, November, and December, of 1901, there was a small epidemic of tetanus after vaccination in Camden, Philadelphia, and to a certain extent in some nearby towns. Camden had 11 cases, and Philadelphia even more than this number. These groups of cases have been adduced as evidence in favor of the view that the tetanus infection is in the virus. Willson, however, shows that there occurred in Philadelphia during the above period 12 cases of tetanus independent of vaccination. In Baltimore during the month of August there were 6 cases of tetanus independent of vaccination, in September 6 cases, and in October (the month in which the Camden outbreak occurred) 8 cases.

In 1899, in New York City, there were 63 deaths from tetanus unrelated to vaccination; in Philadelphia, in 1901, there were 29 deaths from similar cases, and in Cook County, Illinois, from June 25 to July 14, 1900, 27 deaths from tetanus from causes other than vaccination. In 1903 there occurred throughout the United States 406 deaths from tetanus as a result of wounds received on the Fourth of July from toy pistols and blank cartridges (special article in *Journal of the American Medical Association*). These figures indicate that such epidemics of tetanus as occurred after vaccination in Philadelphia and Camden might readily have developed from other causes.

Improper care of the vaccine wound and the development of excessive inflammation and ulceration appear to be important factors in predisposing to tetanus infection. Willson says: "In every instance in the series of cases included in this paper, in which any information could be obtained whatsoever, there has been found some gross breach in the care of the wound, and usually the presence of some active influence that would offer more than a likely means of entrance for tetanus or any other infection." "Nearly every case showed for days a large open ulcer, burrowing deep into the tissues. Two cases were those of soldiers, sleeping anywhere and everywhere, and looking on a bath as a luxury. Several children lived over, and next to and played continually in stables, the hotbed of the tetanus bacillus. One slept in bed every night with her father, who had charge of horses. Two at least are known to have forcibly maltreated the vaccine wound. Many removed the scab for inspection. Two threw or dropped the scab on the ground and replaced it in the wound, one wearing it for hours. One threw his bandage on the ground and replaced it on the arm at a later time. Several wore a shield over the wound without cleansing or removing it until it was full of pus and dirt and foul to smell; one of these reached the eighteenth day and the writer's case the twenty-eighth with the shield still in place. One, when tetanus developed, exhibited a merino shirt-sleeve, that had never been washed, matted in the vaccine wound."

Rosenau,¹ in a study of the bacterial impurities of vaccine virus, was unable to find tetanus organisms in any of a considerable number of glycerinated points and tubes bought in open market and examined with this object in view. He states that tetanus organisms cannot grow or produce their toxin, either in glycerinated virus or on dry points. "It would take gross carelessness to contaminate the vaccine with a sufficient number of tetanus spores to carry the disease to those vaccinated. It is not a matter of surprise that some outbreaks of tetanus have occurred when thousands of open wounds are presented for the reception of this infection so widely distributed in nature."

Considering the hundreds of thousands of vaccinations which are performed each year, and the neglect of the vaccination wound on the part of many persons, the wonder is that not more cases of tetanus develop. Where the vaccinia runs a perfectly normal course, and the vesicle is uninjured and the crust undisturbed, tetanus is much less prone to develop. Tetanus would appear to occur no oftener—if as often—after vaccination than after ordinary cutaneous wounds.

The usual period of incubation of traumatic tetanus is from seven to nine days. The average period of incubation of the reported cases of tetanus after vaccination is twenty-two to twenty-three days. Among Willson's cases, 45 developed tetanus fourteen days or more after vaccination; 31, twenty days or more after vaccination; 1, twenty-eight days after vaccination, and 1, at the end of seven weeks.

The effort has been made to explain the late onset of tetanus by assuming that the tetanus germs lie dormant in the skin until the vaccinia reaches the stage when tissue destruction takes place. It is thus attempted to explain the two weeks' delay in the appearance of the symptoms of tetanus.

In at least three instances in which tetanus followed vaccination the same virus was used upon other persons in addition to the one that developed the disease. In a case investigated by the British Royal Vaccination Commission "a female child, aged two months, developed trismus on the twenty-third day after vaccination. This child was vaccinated from the arm of a female infant, aged five months, and *at the same time and with the same lymph six other children were vaccinated, and none of them developed tetanus or sore arms.*"

In a case of tetanus occurring in a woman aged twenty-one years, reported by Drs. William Findlay and J. W. Findlay,² several people were inoculated with virus from the same tube, but none save the one patient developed tetanus. In one of the Camden cases the patient's "brother was vaccinated from the same tube, the vaccination proving successful and normal." These cases would certainly seem to indicate that the tetanus organisms were not derived from the vaccine virus employed.

Tetanus germs are found in abundance in garden soil and street dirt;

¹ Director of the Hygienic Laboratory of the United States Public Health and Marine Hospital Service, Bulletin 12, 1903.

² *Lancet* February 22, 1902.

they are commonly present in the manure of herbivorous animals, but to a much less extent in the excrement of suckling calves. Huddleston, of New York, found them in 8 per cent. of the calves used in the laboratory of the New York Health Department.

While the contamination of vaccine virus with tetanus germs must be admitted as a possibility, we believe, from a study of the recorded instances of this complication, that the tetanus infection was in the great majority of cases received into the system at a period subsequent to the insertion of the lymph. About three-quarters of the cases of tetanus after vaccination have proved fatal.

Vaccinal Syphilis.—The study of vaccinal syphilis has been bereft of much of its importance since the general adoption of calf-lymph for vaccination. Inasmuch as the bovine species is totally insusceptible to the syphilitic infection, it is obviously impossible to convey this poison by vaccination with lymph from this source. It has been suggested that syphilis might be conveyed in the vaccine virus as a result of a syphilitic vaccinator expelling the lymph through the capillary tube with his breath, but this is a purely gratuitous assumption, entirely without any clinical evidence.

With the employment of humanized virus and particularly with arm-to-arm vaccinations, it must be frankly admitted that, though relatively of extremely rare occurrence, it is possible to convey the syphilitic poison. The infrequency of this lamentable accident may be comprehended when it is stated that Dr. Robert Lee saw but one case of supposed vaccinal syphilis among 30,000 children at the Hospital for Sick Children, Great Ormond Street, London, an institution particularly likely to attract cases of syphilis. At the East London Hospital for Children, Dr. Radcliffe Crocker, although for many years on the lookout for such cases, never observed a single instance of vaccinal syphilis.

In 1856 the London Board of Health collated the experiences and opinions of a large number of prominent physicians concerning vaccinal syphilis. None of the respondents were able to present any convincing facts, and a large majority expressed complete incredulity as to its occurrence. The English Royal Vaccination Commission, referring to this incident, remarks: "It is impossible to believe that an event concerning the possibility of which almost all the leaders of the profession were in 1856 incredulous can be otherwise than extremely rare."

The commission in its judicial sessions examined many physicians who had extensively practised vaccination for many years, and who had never personally observed vaccination syphilis themselves or heard of it in the immediate practices of their colleagues.

Nevertheless, the fact must be admitted that cases of syphilitic infection have resulted through vaccination from arm to arm. While the number of such cases is infinitesimally small when compared with the enormous number of vaccinations performed, the aggregate number of cases of invaccinated syphilis on record throughout the past century is not inconsiderable.

Epidemics of vaccinal syphilis have been observed and reported by Marcolini (1814 in Udine), Cerioli (1812 in Cremona), Tassani (1841 in Grumello), Wegeler (1849 in Coblentz), Oberfranken (1852 in Freienfels), Marone (1856 in Lupara), Pacchiotti (1861 in Rivalta), Depaul (1866 in Morbihan, France), Kocevar (1870 in Schleinitz and St. Veix), Jonathan Hutchinson (1871 in London, two series of cases), and Layet (1880 in Algiers and 1885 in Turin).

A brief account of the Rivalta and Lupara epidemics, which are fairly typical of all the rest, is herewith subjoined:

In 1861 Pacchiotti¹ reported an extensive epidemic of vaccinal syphilis occurring in Rivalta, Italy: 46 children were vaccinated from the original vaccinifer; of these 40 contracted syphilis. From 1 of these subjects 7 other children became infected through vaccination. In addition 20 mothers or nurses contracted syphilis through contact with these children. But 17 out of 63 vaccinées escaped infection.

About the same time Marone² published an account of a similar epidemic that occurred at Lupara in 1856. A large number of infants were vaccinated with humanized lymph received in tubes from Campobasso, and 23 were infected with syphilis. From 1 of these children 11 other infants were inoculated with the disease. As in the Rivalta tragedy, a number of mothers and nurses subsequently developed chancres of the nipple.

It will be seen that more than half of the cases of vaccinal syphilis that have been recorded have occurred in Italy. The remainder have been found in France, Germany, and England. Fortunately, such infections in the United States have been extremely rare. It has been estimated that the aggregate number of cases of vaccinal syphilis that have occurred is about seven hundred. When we think of the millions of lives that have been saved by vaccination during the past century, we recognize the fact that the sacrifices, however deplorable, have been relatively small. Many blessings are leavened with misfortune.

Pacchiotti, in 1861, laid down the following rules to be observed in vaccinating: 1. Enquire into the state of the patient's health. 2. Take the lymph in preference from those children who have passed the fourth or fifth month, as hereditary syphilis appears, in general, before that time. 3. Do not use lymph taken from a vesicle which has passed its eighth day, because on the ninth and tenth days the lymph becomes mixed with pus, which later may be of an infectious character. 4. In taking the lymph, avoid hemorrhage, as there is less danger with lymph free from blood. 5. Do not vaccinate too many children with the same lymph.

The observance of these precautions would obviate much of the risk of transmitting syphilis, but would not confer absolute security against such infection. The British Royal Commission on Vaccination says: "Absolute freedom from risks of syphilis can be had only when calf-

¹ *Sifilide Transmissa per Mezzo Della Vaccinazione in Rivalta Presso Acqui. Gazzetta Della Associazione Med.*, October 20, 1861.

² *Impraziale de Florence*, November 5, 1862.

lymph is used, though where the antecedents of the vaccinifer are fully ascertained, and due care is used, the risk may for practical purposes be regarded as absent."

Inasmuch as bovine virus is at the present time generally and, indeed, almost universally employed, the subject of syphilis may be dismissed in a discussion of the complications of vaccination.

The employment of calf-lymph and the complete elimination of the risk of transferring syphilis to the vaccinée have robbed the opponents of vaccination of one of their most potent arguments against the enforcement of vaccination.

The Relation of Vaccination to Tuberculosis.—Whether or not it is possible to transmit tuberculosis in vaccine lymph is an undetermined question. Toussaint¹ claims to have successfully inoculated rabbits and a pig with tuberculosis with lymph taken from a vaccine vesicle induced upon the vulva of a tuberculous cow. On the other hand, Josserand² injected lymph taken from vaccine vesicles in tuberculous individuals into the peritoneal cavity, under the skin, and into the anterior chamber of the eye in 47 animals. Post-mortem examinations gave absolutely negative results in 43 of these, and in no animal was there conclusive evidence of tuberculosis.

The danger of conveying tuberculosis in bovine lymph is almost inappreciable. The virus is obtained from calves, and it is pretty well established that calves are but rarely the subjects of tuberculosis. It is stated by Fürst, on the authority of Pfeiffer, that but one case of tuberculosis was found among 34,400 calves under four months of age.³ The statistics of the abattoirs of Augsburg and Munich corroborate the above figures; only one tuberculous calf was discovered at Augsburg among 22,230 slaughtered, and a smaller percentage at Munich.⁴

Furthermore, in well-regulated vaccine establishments calves are subjected to the tuberculin test before vaccination, and are autopsied before the lymph is distributed for use. Even though it were possible, despite these precautions, for tubercle bacilli to get into the lymph, they would perish if the lymph were glycerinated. Copeman,⁵ speaking of glycerinated lymph, says: "The tubercle bacillus is effectually destroyed even when large quantities of virulent cultures have been purposely added to the lymph."

Bollinger, Heron, and Acland all seriously doubt whether tuberculosis has ever been transmitted by vaccination.

Postvaccinal Lupus Vulgaris.—Cases of lupus occurring in and around vaccination scars have been reported by Lenander,⁶ Besnier,⁶ Perry,⁷ Little,⁸ Colcott Fox, Acland,⁹ Stelwagon,¹⁰ and others. Most of

¹ French Academy of Sciences, August 8, 1881, quoted by Acland, *Allbutt's System of Medicine*, p. 619.

² *Contribution à l'étude des contamination vaccinales*, Lyons, 1884, p. 30, quoted by Acland.

³ Fürst. *Die Pathologie der Schutz-Pocken-Impfung*, Berlin, 1896, par. 431, p. 112, quoted by Acland.

⁴ Strauss. *Gaz. hebdom. de méd. et de chirurg.*, 1885, p. 143, quoted by Acland.

⁵ *Vaccination, its Natural History and Pathology*, London, 1899, p. 181.

⁶ *Annales de dermat. et de syph.* 1889, p. 576.

⁷ *British Journal of Dermatology*, 1898, p. 196.

⁸ *Ibid.*, 1900, p. 60.

⁹ *Loc. cit.*

¹⁰ *Journal of the American Medical Association*, November 22, 1902.

these observers saw the lupus years after the vaccination had been performed. Fox saw a case of lupus begin in a vaccination scar shortly after the sore had healed. The child subsequently developed a disseminated lupus, subperiosteal tuberculous nodules, and pulmonary phthisis. It is highly probable that this child was already tuberculous, as another child in the family had previously died of this disease. Stelwagon saw a palm-sized patch of lupus on the arm in a girl ten or twelve years after a vaccination which was said to have been immediately followed by the development of the lupus, the history being given by a physician, the brother of the patient. All that can be stated as regards the relationship of vaccination to lupus is that vaccination may in rare cases in tuberculous individuals give rise to a lupus at the site of vaccination. That lupus should occasionally choose a vaccination scar for its seat is no proof that it was caused by vaccination.

Vaccination and Leprosy.—Since the general adoption of bovine lymph for vaccination, the question of the invaccination of leprosy has resolved itself into one of academic and retrospective interest. It is well, however, for physicians in leprosy countries, if required by unusual circumstances to employ humanized lymph, to remember that leprosy has probably in isolated instances been conveyed by vaccination. Gairdner,¹ Daubler,² and Hillis have each recorded instances of vaccinal leprosy, although some doubt attaches to all of these cases.

Beavan Rake and Buckmaster, who have given this matter much study, believe "that the alleged cases of transmission of leprosy by vaccination are open to serious doubt." Hansen,³ of Bergen, in 1890, made extensive inquiry by circular to all of the physicians of Norway as to the occurrence of vaccination leprosy. In not a single case was there any ground to suspect such an origin. This statement is of especial importance inasmuch as there is much leprosy in Norway, and vaccination is practised extensively in that country.

From experimental evidence we would scarcely expect leprosy to be transmissible by vaccination. Inoculation of man and lower animals has been repeatedly attempted by Daniellson, Profeta, Hansen, and others, who inserted fragments of leprosy tissue and injected blood from lepers beneath the skin, but with entirely negative results. There is indeed no conclusive case on record of the successful experimental transmission of leprosy.

It is true that lepra bacilli have occasionally been found in vaccine lymph in vesicles raised upon leprosy skin, but, as Beavan Rake properly states, no responsible person would think of vaccinating a leper in an affected part and using such lymph for further vaccinations.

Eczema Following Vaccination.—Vaccination may now and then induce the appearance of an eczema in a child predisposed to the disease, just as an attack of measles, scarlet fever, or simple teething may act as an exciting cause. Eczema is an extremely common disease

¹ A Remarkable Experience Concerning Leprosy. *British Medical Journal*, 1887, vol. 1, p. 1269.

² *Monatsh. f. prakt. Derm.*, 1889, p. 123.

³ Mentioned by Acland, *Allbutt's System of Medicine*, p. 625.

among infants and young children, and is particularly referable to faulty feeding and digestive disturbances. Of 600 cases of eczema under the care of Dr. T. Colcott Fox, 249, or 41.5 per cent., were seen before the end of the first year; in 40 of these eczema was known to have appeared before vaccination. Doubtless if these had appeared after vaccination, the latter would have been viewed as a probable etiological factor.

Crocker¹ says: "In no case can vaccination be held responsible where the vaccinia pustule has completely healed before eczema appears."

Eczematous children, if in good health otherwise, may usually be vaccinated without any aggravation of the existing cutaneous disease. Van Harlingen² has carefully studied the influence of vaccination on previously existing skin diseases. He writes: "During the smallpox epidemic of 1872 I observed all cases of skin disease coming under my notice in which vaccination had been practised. In a few some aggravation of the symptoms followed; in others an apparent improvement took place. But in the great majority of cases vaccination did not appear to exercise any influence whatever on the course of the more common diseases of the skin coming under my observation." We have from time to time vaccinated persons with eczema and other cutaneous diseases without any injury whatsoever. On the other hand, vaccination has on a number of occasions been followed by improvement and even cure of eczemas. Stelwagon³ says: "I have noted in several instances that amelioration followed vaccination, and in one instance, in a chronic case, a disappearance of the eczema." Duhring, Tait, and others have testified to the occasional curative influence of vaccination on eczema.

While we would not elect to perform vaccination upon a child suffering from eczema, we should not consider the latter condition a sufficient contraindication if smallpox were prevalent.

Bullous Eruptions (*dermatitis bullosa*; *dermatitis herpetiformis*; *acute pemphigus*).—In relatively rare instances vesicobullous eruptions variously designated as pemphigus, bullous dermatitis, and dermatitis herpetiformis (Duhring's disease) have followed vaccination. While we have no proof positive of a causative relationship between vaccinia and these eruptions, they have now been reported by careful observers in a sufficient number of instances to warrant the assumption that the antecedent vaccination has been of some etiological moment.

Pusey⁴ reported a case of this character under the title of dermatitis herpetiformis, in which the lesions were vesicobullous and erythematous, followed by pigmentation.

Dyer⁵ reported two similar cases under the same title after vaccination. One case occurred three weeks after vaccination and one several (?) weeks thereafter.

¹ Diseases of the Skin, p. 324.

² Remarks on Vaccination, in Relation to Skin Diseases and Eruptions Following Vaccination, Philadelphia Medical Journal, 1902, p. 184.

³ Vaccinal Eruptions, Journal of the American Medical Association, November 22, 1902.

⁴ Journal of Cutaneous and Genito-urinary Diseases, 1897.

⁵ St. Louis Medical Gazette, 1898.

Bowen¹ has placed on record a series of six cases of bullous dermatitis resembling dermatitis herpetiformis following vaccination. In three of the cases the eruption is stated to have made its appearance within two weeks after vaccination, in one within a week, while in two it did not show itself until after the lapse of a month. Corlett exhibits two photographs of postvaccinal bullous dermatitis in his work on the acute infectious exanthemata. Stelwagon² saw within one year three cases of bullous eruption after vaccination, two of which he regarded as *acute pemphigus*, and the third as a persistent bullous erythema multiforme or dermatitis herpetiformis. In these cases the vaccination was what is usually described as a "good take," but was somewhat slow in healing, the crust remaining adherent a long time. The eruption appeared from two to four weeks after vaccination, and had persisted at the time they were reported three, four, and eight months, respectively.

Sequeira³ showed to the Dermatological Society of London in 1902 a case of *pemphigus* in a man aged thirty-nine years, the eruption appearing three weeks after a revaccination. Three vaccine insertions were made, and the first bleb is alleged to have developed at the site of one of these. This was followed in several weeks by bullæ on the arms, and later on the thighs. Cultures from the early blebs were sterile, and inoculations of this fluid into animals were negative.

In all of the above cases save the last, the patients were children under twelve years of age. The eruption usually appeared from two to three weeks after vaccination, and in no case after six weeks. In most cases the eruption was extensive and of long duration, with marked tendency to relapse. Some of the cases were cured at the end of three or six months, but some persisted much longer. Pusey's case continued to have relapses for four and a half years.

Bowen says: "The chief features that these cases present in common, and that lead to a conviction that they have a common etiology, are their occurrence in children after vaccination; their course, varying from several months to several years or perhaps longer; their uniformly vesicular and bullous character, with only occasional evidences of multiformity; the almost complete exemption of the trunk; the characteristic grouping about the mouth, nose, ears, wrists, ankles, and feet, and the very slight prominence of itching or other subjective symptoms." While most of these cases run a relatively benign course, one of the writers⁴ saw a fatal termination in a case of bullous eruption of the acute pemphigus type. This occurred in a girl of five years, the eruption beginning two weeks after vaccination. The writers have also seen four other cases of generalized bullous eruption of the type described above, occurring shortly after vaccination.

A remarkable series of bullous eruptions occurring after vaccination

¹ Journal of Cutaneous and Genito-urinary Diseases, September, 1901, p. 101.

² Journal of the American Medical Association, November 22, 1902.

³ British Dermatological Journal, May, 1902, p. 174.

⁴ Schamberg and Keech. A Case of Acute Fatal Pemphigus, Annals of Gynecology and Pediatrics February, 1901, p. 321.

is reported by Howe,¹ of Boston. Ten cases are referred to, all but one occurring in persons who had been recently vaccinated. The skin lesions began on an average of five weeks after vaccination; the longest time elapsing between vaccination and the appearance of the eruption was sixteen weeks, and the shortest period three weeks.

All of the patients were adults, the ages varying from twenty-one to fifty-two years. Six of the ten cases proved fatal; the average duration until recovery or death occurred was six weeks.

It will be seen that these cases present points of variation from the cases described by Bowen. The interval between vaccination and the appearance of the eruption in Bowen's cases was about two and a half weeks; in Howe's cases it was double this period. Bowen's cases occurred in children; none of them were fatal, and the trunk was, as a rule, free of eruption, which was not true in the cases described by Howe.

Howe was inclined to attribute the eruptions to infectious material introduced at the time of or after vaccination. The cases occurred at a time when smallpox was prevalent in epidemic form, and when thousands of vaccinations were being performed.

While these eruptions, when compared with the number of vaccinations performed, are extremely rare, no effort should be spared to determine their cause with a view to their future avoidance. It is possible that they are manifestations of an extraneous infection through the vaccine wound. In this connection the investigations of Pernet and Bulloch² into the causation of acute pemphigus are of interest. These writers report and analyze eight cases of acute pemphigus in butchers; six of the cases proved fatal in from twenty-four hours to eighteen days. Three patients gave histories of wounds which continued to suppurate up to the time of the pemphigus outbreak. The period of incubation would appear to be very long if the disease arose from an infection, as is suggested. In the three cases referred to the wound antedated the eruption three months, two months, and five weeks, respectively. Special interest attaches to one case, in which the patient is alleged to have inoculated himself by contact with a bullous eruption on the udders of a cow.

Psoriasis.—Psoriasis is known to have made its first appearance at the point of vaccination, and also as a generalized outbreak after vaccinia. No one, however, who is at all familiar with this disease would look upon vaccination as a cause of psoriasis. It may simply determine the time of outbreak in an individual predisposed to this common skin affection; it is quite possible that those persons who developed psoriasis after vaccination would not have been attacked with this disease until a later period. The occurrence of postvaccinal outbreaks of psoriasis has been noted by Klamann,³ 1 case; Campbell,⁴ 1 case; Rohé,⁵ 2 acute general cases of psoriasis after vacci-

¹ Cases of Bullous Dermatitis Following Vaccination, *Journal of Cutaneous Diseases*, 1903, p. 254.

² *British Journal of Dermatology*, 1896, pp. 157 and 205.

³ *Jahrbuch f. Kinderheilk.*, 1879, Bd. iv. p. 371.

⁴ *Arch. f. Derm.*, 1877, p. 311.

⁵ *Journal of Cutaneous and Genito-urinary Diseases*, 1882-83, p. 11.

nation; Piffard,¹ 1 case; Wood,² 2 cases; Hyde,³ 1 case; Gaskoin,⁴ 5 cases; Chambard,⁵ 1 case; and Rioblanco,⁶ 1 case.

Furunculosis.—Crops of boils have occasionally been observed during the course of and following vaccination. The complication is usually a trivial one, the furuncles disappearing in a short time. Sinigar⁷ met with 21 cases of furuncles among 1160 vaccinations in a large institution. The boils developed, as a rule, late in the course of the vaccinia. One case appeared on the tenth day, 1 on the sixteenth, 4 on the twenty-second, 1 on the twenty-fifth, 2 on the twenty-seventh, 2 on the twenty-eighth, 4 on the twenty-ninth, 3 on the thirtieth, and 3 on the thirty-fifth day after vaccination. As bearing on the cause of this complication, it is interesting to note that 13 of these cases developed among epileptics, who, as Sinigar remarks, include some of the dirtiest and most troublesome patients in the asylum.

HISTOLOGY OF THE VACCINE LESION.

But little literature is available upon the subject of the histological changes in the vaccine pock. The following description is condensed from Copeman's⁸ presentation of the subject:

The vaccine lesion passes through three more or less defined stages—namely, papule, vesicle, and pustule—just as does the characteristic lesion of smallpox. In both diseases the *papule* results from inflammatory changes which are most pronounced in the epithelial cells of the mucous layer of the epidermis. Through certain degenerative processes, the most conspicuous of which are cell liquefaction and intercellular œdema, the papule becomes converted into a vesicle.

The vesicle is made up of numerous loculi or compartments which are formed by the spinning out of elongated epithelial cells. The more pronounced swelling and vacuolation of the cells upon the advancing edge of the vesicle leads to greater bulging upon the periphery, giving rise to the *umbilication*. The process is identical in vaccine and varicellous vesicles.

Kent⁹ examined a series of vaccine vesicles removed by Copeman at various stages of development from the calf. At a quite early stage an outpouring of leukocytes occurs toward the site of injury. In the course of time each bloodvessel is surrounded by a mass of leukocytes which rapidly increase and convert the originally transparent fluid of the vesicle into a purulent fluid, thus giving rise to the *pustule*.

The rupture of the epithelial trabeculæ or partitions converts the multilocular pock into a unilocular one. The fluid now gradually becomes inspissated and with the necrosed remains of epithelial cells dries into a *crust*. Cicatrization and healing go on beneath the crust;

¹ Journal of Cutaneous and Genito-urinary Diseases, 1882-83, p. 119.

² Ibid., p. 161.

³ Ibid., p. 14.

⁴ On Psoriasis or Lepra, 1875, p. 49.

⁵ Annales de dermat., 1895, p. 498.

⁶ Ibid., p. 880.

⁷ Vaccinal Complications, Lancet, 1902.

⁸ Loc. cit., p. 73.

⁹ British Medical Journal, 1891, vol. II, p. 633. Quoted by Copeman.

the depth of the resulting scar depends upon the extent of destruction of the true skin.

The minute histological changes in the vaccine lesion have been studied by Gustav Mann,¹ for whom Copeman excised lesions at different stages of development from the calf.

In a specimen removed within an hour after vaccination the wound is blocked by a clot which externally is of a coarse, granular nature, and between the edges of the epidermis finely granular. The bloodvessels close to the injury are dilated and many completely thrombosed with leukocytes. Red corpuscles may be seen adhering to the lumen of the capillaries and arteries.

The nuclei of both the epidermal and dermal cells are swollen and the basophile chromatin contained in them is doubly increased. In the dermis an infiltration of leukocytes into the loose connective tissue is visible.

At the end of twenty-four hours the epithelium close to the injury has increased twofold or threefold in thickness and a characteristic phenomenon is already noticed, namely, the formation of Guarnieri's supposed parasites. The nuclear and nucleolar chromatin is increased and a considerable portion of the latter leaves the nucleus and is found lying free in the cytoplasm. The granules may fuse and give rise to more or less solid spheres lying alongside of the nucleus or even indenting it.

From the twenty-fourth to the forty-eighth hour the dermis shows a gradually increasing œdema, associated with an emigration of leukocytes. As a result of the œdematous condition the lymph is prevented from escaping downward by the dense elastic layer of the dermis and the thick fibrous bundles of the hypoderm. Toward the periphery the lymph channels are blocked by leukocytes, and there is left but one path for the lymph, namely, through the basal membrane and then through the spaces between the epithelial cells. These lymph spaces are distended by the fluid, which becomes limited by the dense and resistant horny layer.

At the end of three days three zones may be distinguished. Farther away from the line of inoculation the only noticeable change is a dilatation of the interepithelial lymph channels. All of the cells immediately within this region, save the horny cells, are swollen and contain granules like those in the granular layer, thus indicating a premature aging of the cells.

The dermis beneath forms large bullæ, the walls of which are made up of compressed connective-tissue cells and leukocytes. No wandering cells are seen in the blebs, but fairly numerous bacilli singly and in pairs.

Still nearer the point of inoculation the epithelial cells show enlarged nuclei, which undergo fragmentation into six or twelve smaller nuclei. Concurrently with the formation of these multinucleated giant cells there are seen greatly distended lymph vesicles in the epithelium, the

¹ Quoted by Copeman, loc. cit.

walls of which are made up of stretched and degenerated epithelial cells. The vesicles contain a fibrin reticulum and various micro-organisms.

Internal to the zone just described the giant cells are replaced by cells but a fifth to a quarter of their size, and containing but one or two nuclei, which appear to be derived from the multinucleated giant cells. The centre of the vaccinated area shows no living epithelial cells, but merely the remains of the horny layer and a dense, dried blood clot.

The above changes hold good for the fifth day, the only difference being an increase in size of the central necrosed area and a lateral spreading of the zone of infection.

The increased infiltration of leukocytes causes the central area to necrose more and more, the connective-tissue elements succumbing to the pressure exerted by the wandering cells.

The hypoderm shows, especially about the fifth day, a considerable swelling of the thick, white, fibrous bundles called forth by the great activity of the fixed connective-tissue cells.

Copeman considers the most characteristic feature of vaccination to be the appearance, immediately outside the necrosed area in the superficial, loose dermal tissue, of a number of globular masses, varying in size and arranged singly or in pairs, and which are colored by a special staining process. At the spreading edge, very short bacilli are seen.

It is suggested that the large globules represent either a capsulated, sporulated, or involuted stage of the bacillus which Copeman elsewhere intimates may be the specific microbe of the disease.

Much that pertains to the bacteriology of vaccinia will be found in the chapter on the pathology of variola.

Tyzzar¹ made a careful experimental study of vaccination and variolation lesions in animals, particularly with reference to the presence of Guarnieri's bodies. He successfully inoculated the corneas of twenty-five rabbits with vaccine lymph, and the corneas of twenty rabbits with variolous lymph. In addition a number of calves were vaccinated, some upon the cornea and others upon different parts of the cutaneous and mucous surfaces.

He interprets the cycle of development of the cytorrhcytes variolæ in vaccinia as follows:

Infection: Epithelial cells are invaded by small forms in which it is difficult to distinguish structure. These small forms are found between cells and in various parts of the cytoplasm, but after their entrance into the cell they take a position near the nucleus. *Growth:* After becoming located near the nucleus they become larger, and with this growth the character of their structure becomes apparent. They then consist of a reticular protoplasm in which is a clear spot containing a mass of basic staining material. Although it is impossible to distinguish a nuclear membrane bounding this clear spot, it seems probable that this clear spot with the granule in it is the chromatin of the organism. The

¹ The Etiology and Pathology of Vaccinia, Journal of Medical Research, February, 1904.

organism is situated in a space in the cell, generally many times its own volume. This space is usually continuous with or is a part of the perinuclear space. *Division of the Nuclear Material*: Certain forms, in which the chromatin mass is irregular, precede those in which the chromatin is divided. In the latter the chromatin granules may be few or numerous. The chromatin granules later take a peripheral position, where they then form the centres of minute masses which bulge from the surface. *Multiplication*: These small masses, becoming free, are found in the space occupied by the segmenting form and in the cytoplasm of the same cell. They constitute the small forms described as the first of the series. They now scatter and penetrate neighboring cells. The invasion of the surrounding normal cells by the small forms resulting from this multiplicative process constitutes autoinfection, and by it the process extends. The immediate effect of the parasite is to cause an increase in size of the epithelial cells. This increase in cell volume is accompanied in the corneal lesion by proliferation. The exudation which usually accompanies the lesions is secondary to the degeneration of the epithelium. Tyzzer states that he is "fully convinced that the vaccine body is an organism and represents the etiological agent in this disease."

THE BLOOD IN VACCINIA.

There is a constant leukocytosis during vaccination, the leukocytosis appearing in two waves, according to Sobotka.¹ The primary one (varying from 12,000 to 23,000) is observed from the third to the seventh day, and a secondary wave (10,000 to 17,500) from the tenth to the twelfth day.

Billings² states that no changes are exerted upon the hæmoglobin or red cells by vaccination, but a definite leukocytosis is produced. The counts average about 15,000 leukocytes per cubic millimetre. The maximum of the leukocytosis is reached during the height of pustulation of the vaccine lesion, after which a gradual diminution in the white cells takes place.

¹ Zeitschr. f. Heilk., 1893, Bd. xiv. p. 349.

² Medical News, 1898, vol. lxxiii. p. 301.

CHAPTER II.

THE RELATIONSHIP OF COWPOX OR VACCINIA TO SMALLPOX.

It has taken almost a century of experimentation to prove the truth of the statements, made by Jenner in his first publication, that smallpox and cowpox were modifications of the same disease. What a tribute to the intuitive discernment of this great man!

The experiments which have led to the general (although not universal) acceptance of this view have been in the direction of the conversion of smallpox into vaccine by variolation of the cow. It is impossible to produce in the cow a generalized eruption similar to the smallpox eruption in man; it is, moreover, impossible to intensify the virulence of cowpox and convert it into smallpox, but it is possible to convert the virus of human smallpox into vaccine virus by passage through the bovine species.

The English Royal Commission on Vaccination presents in its official report (1898) a valuable review of this subject, from which we freely abstract.

Most of the endeavors to transfer smallpox from man to the bovine species have been unattended with success, and have usually been without any definite result. This has been true not only in attempts to produce the disease by infection through the respiratory and digestive tract, but also in many instances by direct inoculation. Most of the inoculation experiments may be grouped in three categories.

The first class includes experiments in which inoculation of smallpox matter into the cow produced a vesicle identical with or closely resembling the vesicle produced by vaccine inoculation. If a typical vesicle was not produced at the first inoculation, the transference of the material from the first vesicle would in a second or third remove in the cow give a typical vesicle capable of producing in man results indistinguishable from ordinary vaccination. Such experiments were carried out by Thiele (1838), Ceeley (1840), Badcock (between 1840 and 1860), Voigt (1881), Haccius and Eternod (1890), King (1891), Simpson (1892), and Hime (1892).

In the second category belong the experiments performed by Klein and Copeman. Klein, who in 1879 had apparently failed in thirty-one attempts, subsequently found, in 1892, that the result of the first inoculation in the cow of smallpox matter was not a distinct vesicle, but merely a thickening and redness of the wound. Lymph pressed from the thickened wound produced, when inoculated into a second animal, a similar but more pronounced result. In the third and fourth cow the reddening and thickening were still greater. Lymph squeezed

from the wounds of the fourth cow produced typical vaccinia in a child, and the crust from the child when reinoculated into the cow produced similar vaccine vesicles. Copeman obtained results of a similar character, and succeeded in the third remove in the cow in producing a reaction which showed commencing vesiculation.

In the third class may be placed the results obtained in an elaborate investigation conducted by a commission of the Society of Medical Sciences of Lyons, under the direction of Chauveau (1865). Their results may be briefly summarized as follows:

Inoculation of the cow with smallpox matter in any one of the thirty animals experimented upon did not give rise to a vaccine vesicle. Nevertheless a definite result was obtained in the form, not of a vesicle, but of a thickening and inflammation of the wound; when a puncture was made this became a papule. Lymph squeezed from such a papule and inserted into a second animal gave rise to a like papule; and this, again, might be used for a third animal, but often failed; and the effect could in no case be carried through more than three or four removes. When the inoculation was repeated on an animal in which a previous inoculation had produced such a papule, no distinct papule was formed, and, moreover, lymph squeezed from the seat of inoculation produced no effect at all when used for subsequent inoculation of another animal.

Thus Chauveau and his commission found that smallpox implanted in the cow gave rise to a specific effect which was not cowpox, but was of the nature of smallpox, though its manifestations in the cow were different from those of smallpox in man. Lymph from the lesions in the first cow was capable of producing smallpox in the human subject.

It is evident from the above experiments that the results obtained from attempted variolation of the cow have exhibited marked variability. The vast majority of the inoculations have been of a negative character. These, however, do not invalidate the positive results which have now attained a very considerable number, and which have been reported by careful and trustworthy investigators at different times and in different countries.

When reaction does result from the insertion of variolous material into the cow, the local effects vary somewhat. There may be directly produced a typical vaccine vesicle, or, as occurs in most instances, a papule or inflammatory induration which on further inoculation yields a vaccine vesicle. We are thus forced to the conclusion that *smallpox is converted into cowpox by passage through the tissues of the bovine species*. The transformation is at times sudden and complete, at other times gradual and incomplete, and sometimes fails altogether. The circumstances which favor such a conversion are but little understood, although it would appear that the youth of the inoculated animal is a factor. The best results have been obtained with calves not over three or four months old.

It is claimed that it is possible for cows to develop cowpox through inhalation of the contagium of variola. In this connection it is interesting to refer to an occurrence noted by Ceely in 1840. This writer

states that he observed cowpox develop in five out of eight milch cows twelve to fourteen days after they were seen licking some flock from a mattress upon which a patient died of confluent smallpox, and which had been spread upon the ground to be aired. Careful investigation revealed the fact that the animals, which had been on the farm for considerable time, were in good health before their admission to the pasture where the exposed bedding lay. There had not been any cowpox in the neighborhood. That the cowpox may have resulted from a volatile contagium derived from the smallpox-infected bedding is not improbable, in view of the simultaneous sickening of the cows after a period of incubation of about two weeks. The possibility of infection through the digestive tract, which Chauveau and others have shown may take place, must not be entirely eliminated in seeking the explanation of the manner in which the disease was received.

That the transformation of the smallpox into the vaccine virus is frequently a gradual process which is not completed in the first bovine inoculation has been on more than one occasion unfortunately proven by the transference of true smallpox to persons who were vaccinated with material taken from the first cow.

In 1836 J. C. Martin, of Attleborough, Massachusetts, inserted into the udder of a cow lymph taken from a smallpox lesion upon the body of a man who died of variola. Subsequently matter derived from the cow was inserted into the arm of about fifty persons. Nearly all of these individuals developed smallpox in the due course of time, and three of the number died. The disaster so preyed upon the mind of the unfortunate physician that he became insane.

A similar occurrence has been reported by Dr. Thomas F. Wood.¹ We quote his own words: "I had occasion just after the war (1865-66), while in charge of the Wilmington Smallpox Hospital during an epidemic of the disease, to go over the same ground of attempting the production of artificial cowpox. It happened, during the progress of the experiment that an army medical inspector, whose name I have forgotten, was making a tour of the hospitals; hearing of my experiments, he visited my hospital and after examination pronounced the small vesicles genuine cowpox, and confirmed his faith in his opinion by making some inoculations on the arms of two children in an Irish family near by. The inoculations resulted in a genuine smallpox, which went through the family in various grades of intensity."

Other instances of a similar character have been recorded. That such infections are not the result of inoculation with the unchanged variolous material originally introduced into the cow is evidenced by the fact that smallpox has been conveyed to the human subject from a papule of the second remove. (Lyons Commission.)

These deplorable accidents have directed attention to the unwisdom of using material of the first or second bovine generation, and emphasize the importance of passing the variolous virus through four or five or more animals before employing it upon man.

¹ Chicago Medical Journal and Examiner, October, 1881.

The demonstration of the fact that vaccine virus may be produced from a variolous source is of great importance. It is readily seen that an epidemic of smallpox occurring in some inaccessible country, where active vaccine lymph could not be obtained, could be made to supply the material for its own suppression.

The proof of the common ancestry of vaccinia and variola refutes the theoretical arguments advanced by Crookshank and others against the protective influence of vaccination. These writers have attempted to fortify their belief in the inefficacy of vaccination by assuming the duality of these two affections, the opinion being maintained that an attack of disease could only afford protection against the same disease. The premise being false, the entire inference falls to the ground.

Modern bacteriological research strongly supports the empiric discovery of Jenner. Pasteur and others have shown that it is quite possible, by the use of an attenuated virus, to produce a mild attack of an infectious disease and thus protect against a more severe type of the same infection.

That vaccinia and variola are in *essence* the same disease is scarcely to be doubted. The passage of smallpox matter through the comparatively insusceptible tissues of the bovine species attenuates the virus to such an extent that it is permanently robbed of the virulence which it once possessed. Instead of producing a dangerous and contagious disease, it gives rise to an innocent affection capable of transmission only by inoculation, and having the beneficent property of protecting against the original disease which gave it birth. Shakespeare might well have had vaccination in mind when he wrote:

"Take thou some new infection to thine eye,
And the rank poison of the old will die."

Jenner was strongly impressed with the fact that smallpox and cowpox were one and the same disease. Baron quotes the following notes which were left by Jenner in one of his journals:

"The origin of the smallpox is the same as that of the cowpox; and as the latter was probably coeval with the brute creation, the former was only a variety springing from it." Cowpox and smallpox are "*not bona fide dissimilar* in their nature; but, on the contrary, *identical*. On this ground I gave my first book the title of '*An Inquiry into the Causes and Effects of the Variolæ Vaccinæ*'—a circumstance which has been since regarded by many as the happy foresight of a connection which was destined by further evidence to become more warranted."

From the above it will also be seen that Jenner regarded cowpox as the progenitor of human smallpox. This belief he reiterated on a number of occasions. It will be remembered that in the beginning of the "Inquiry" he says: "This fluid (from the *grease*) seems capable of generating a disease in the human body (after it has undergone the modification I shall presently speak of—viz., transmission through the cow) which bears so strong a resemblance to smallpox that I think it highly probable that it may be the source of that disease." Again, in a

letter to De Carro in 1803 he remarks: "I am happy to find an opinion taken up by me and mentioned in my first publication has so able a supporter as yourself. I thought it highly probable that the smallpox might be a malignant variety of the cowpox, but this idea was scouted by my countrymen, particularly P. (Pearson) and W. (Woodville)."

Whether smallpox is a cowpox of exalted virulence or cowpox an attenuated smallpox remains apparently unsolvable. Copeman is inclined to support the view championed by Jenner. He says:¹ "The artificially inoculated form of cowpox which we term vaccinia is nothing more nor less than variola modified by transmission through the bovine animal. Perhaps the most reasonable interpretation of such results may be that smallpox and vaccinia are both of them descended from a common stock—from an ancestor, for instance, which resembled vaccinia far more than it resembled smallpox. It is conceivable, indeed, that the seeming vaccinia, obtained in the calf by inoculation of smallpox matter into that animal, may after all be but a reversion to an antecedent type."

The Various Natural Sources of Lymph.—During the investigation of the casual cowpox, Jenner conceived the idea of propagating the disease by inoculation after the manner of the smallpox, first from the cow, and finally from one human being to another. The first vaccination was performed in 1796 upon a lad by the name of James Phipps, the virus being taken from the hand of Sarah Nelmes, a dairymaid who had been accidentally infected with the cowpox. Notwithstanding the resemblance of the vesicle produced to that obtained by variolous inoculation, Jenner could scarcely believe that the patient was secure from the smallpox. He was, however, inoculated with smallpox virus some months afterward and on numerous occasions subsequently, but each time without result.

In 1798 Jenner again came into possession of virus from the cow and made arrangements for a series of inoculations. "A number of children," he says, "were inoculated in succession, one from the other; and after several months had elapsed they were exposed to the infection of smallpox, some by inoculation, others by variolous effluvia, and some in both ways, but they all resisted it."

This strain of lymph was suffered to die out and none was found until Woodville, in 1799, discovered a case of natural cowpox in Gray's Inn Lane. With this lymph he vaccinated seven persons, and likewise certain others from the hand of a dairymaid who had contracted cowpox from one of the cows at this place. This virus was successively passed through hundreds of persons and became known as "Woodville's lymph."

Dr. Pearson also discovered a case of cowpox in a dairy at Marylebone Road, although some of the lymph which he sent out was probably obtained from Woodville's cases. Woodville and Pearson both distributed the lymph widely, and supplied it to many of the continental

¹ Vaccination, London, 1899, p. 64.

cities. Although Jenner himself used some of Woodville's lymph, he later found another source of supply in the dairy of Mr. Clark, in Kentish Town.

Dr. Waterhouse, of Boston, secured some of Jenner's lymph through Dr. Haygarth, of Bath, who obtained it from Mr. Creaser. De Carro of Vienna, Stromeyer of Hanover, and others also obtained some of the Jennerian stock.

At this time other instances of natural cowpox became known. Sacco, a faithful disciple of Jenner, discovered a case of cowpox on the plains of Lombardy in 1800. A strain of lymph was developed from this, some of which was sent to De Carro, at Vienna. This enthusiastic vaccinator forwarded a supply to Constantinople, and subsequently other lymph of Italian origin to India; the latter virus was of equine ancestry, having been developed by Sacco from a case of accidental horsepox in a coachman.

Natural cowpox is said to have been found in Naples in 1812, and in Piedmont in 1830. Macerdoni discovered it in cows of Swiss breed in Rome in 1832 and 1834, and in the latter year a lymph stock was established. Cowpox occurred in Würtemberg in 1802, and in 1812 Bremer observed it in Berlin. Fischer saw a case near Luneberg, and Mende noted one in Greifswalde. Giesker, Luders, Ritter, Riss, and Albers encountered cases in various portions of Germany. Numann says that in Holland cowpox was seen in 1805, 1811, and 1824.

An epizootic of this disease among cows is said to have occurred in Russia in 1838, in a small village near St. Petersburg.

In France cowpox was first observed in 1810 in the department of La Meurthe; in 1822 it was found in Clairvieux. In the next half-century it was discovered some score or more times in different parts of the country.

A famous strain of lymph was derived by Bousquet in 1836 from a case of cowpox at Passy, in the environs of Paris. The disease occurred upon the hand of a dairymaid, from whom Bousquet vaccinated a number of children. In the second and subsequent removes, the virus proved itself much superior to the lymph which had then been long in use. Bousquet in a painstaking memoir accurately compared the course of the old and the new lymph. These results were confirmed by Bruchir, of Versailles, and by Steinbrenner, who worked with Mrs. Pass's lymph in 1840, and compared it with virus obtained from other sources in 1841 and 1845. Similar results were obtained by Estlin, of Bristol, in 1838 with lymph derived from a Gloucestershire farm.

Don F. Xavier Balmes, director of the Spanish Vaccine Expedition, discovered cases of natural cowpox in the Peruvian Andes and in other regions of South America.

Ceely, in 1841, stated that he had experimented with lymph from more than fifteen sources, six of which represented cases of natural cowpox.

In 1866 a milch cow with cowpox was discovered at Beaugency, France. A valuable strain of lymph was developed from this case by Professor Depaul. It was from this source that Martin, of Boston,

obtained lymph with which he inaugurated animal vaccination in America in 1870. It may be worth while to state the great probability that in America only has the "stock" of the Beaugency virus been perpetuated.

The strain of lymph now used by the English Government Animal Vaccine Establishment was derived in 1881 from a case of cowpox at Lafôret, near Bordeaux.

In 1881 Martin, of Boston, observed a case of spontaneous cowpox at Cohasset, a small town in Massachusetts. The Cohasset and the Beaugency stocks were for a while propagated separately in this country, but subsequently became mixed.

Fischer and Voigt in Germany, Haccius in Switzerland, King in India, and others have of late years propagated cowpox virus by variolating heifers, producing thus what has been called variola-vaccine lymph.

We are conscious of a reassuring sense of security in the knowledge that reliable vaccine lymph can be produced by the inoculation of various material into a succession of bovine animals, for if existing strains of lymph are lost or become too much attenuated, we have at hand a means of replenishing the prophylactic virus.

Animal Vaccination.—By the term animal vaccination is meant the propagation of lymph through successive series of calves or heifers, the original virus being derived *ab initio* from a case of spontaneous cowpox. Martin¹ says the term can and has been applied to: 1. Vaccination casually or intentionally from the original spontaneously occurring disease in the milch cow. 2. Retrovaccination with virus obtained from the vaccine disease in the human subject. 3. From vesicles, said to be vaccine vesicles, obtained by variolation of kine, or the inoculation of bovine animals with the virus of smallpox. 4. The method of true animal vaccination, or the inoculation of a bovine animal with the virus of original spontaneous cowpox; from this another, and so on in continuous and endless series as a source of vaccine virus.

In 1810 a Neapolitan physician, Galbiati by name, published an article advocating animal vaccination. He had employed this method for some seven years, believing that it ensured greater vigor and purity of the lymph. Galbiati seems to have espoused this procedure because of the occasional transmission of syphilis by arm-to-arm vaccination. The method was at first extremely unpopular, and its author, abused and ridiculed, is said to have become insane and to have ended his life by suicide. His disciple and successor, Negri (to whom Ballard gives credit for the origin and introduction of animal vaccination), continued the propagation of lymph from animal to animal, and successfully brought the practice into general favor. The lymph which he employed at first (in 1842) appears to have been of human origin, but subsequently he obtained material from a case of natural cowpox in Calabria. Palasciano, a townsman of Negri and a strong advocate of animal vaccina-

¹ Report on Animal Vaccination, read before the American Medical Association, 1877. We are indebted for much of the information conveyed in this chapter to this admirable report.

tion, disseminated knowledge on this subject throughout Europe, by an address before the Medical Congress of Lyons. A young French physician, Lanoix, one of those present, became greatly interested in the subject and subsequently went to Naples to study animal vaccination under Negri. In 1864 he returned to Paris with a heifer which had been vaccinated at Naples. Chauveau and Diday were permitted to take some lymph from this animal at the Lyons railway station. Lanoix proceeded to Paris and in company with Chambon established a private institution for the propagation of animal lymph. The new practice excited considerable interest, and the Academy of Medicine, encouraged by a government appropriation, appointed a commission with Professor Depaul at its head to investigate the subject. The report was favorable to animal vaccination, although some dissentient opinions were expressed. About this time natural cowpox was discovered at Beaugency, and Depaul had an opportunity of employing lymph from this source. It is said that this lymph stock was lost during the siege of Paris in the Franco-Prussian War, and that the only extant derivative from this source is that sent to America.

From Paris the practice of animal vaccination spread to Belgium through the efforts of Warlomont, who obtained some Neopolitan lymph from Lanoix. He later, in 1868, discovered a case of spontaneous cowpox at Esneux (Liège).

Through private enterprise animal vaccine establishments were organized in the various European capitals. The commercial spirit rendered a real service to humanitarian science.

Pissin opened up such an animal vaccine institution in Berlin, and Vienna soon had a similarly equipped establishment. Haccius in 1882 founded the "Institute Vaccinale Suisse," which received a certain recognition at the hands of the Swiss government. Paris now has an "Institut de Vaccine Animale," which under the direction of Chambon and St. Yves Ménard, supplies the municipality with all the lymph required for public vaccinations.

In Germany all or nearly all of the vaccine establishments are under governmental control and supervision.

England in 1881 authorized the founding of the Government Animal Vaccine Establishment in Lamb's Conduit Street, and the use of animal lymph has now practically superseded arm-to-arm vaccination.

To Dr. H. A. Martin, of Boston, belongs the credit of introducing animal vaccination into the United States. In 1870 he sent a special agent to France, who returned with an abundant supply of Beaugency lymph. Having secured a herd of young, healthy animals, he at once began the propagation of animal lymph. He and his son subsequently discovered a case of spontaneous cowpox in Cohasset, Massachusetts.

Advantages of Animal Vaccination.—The use of calf-transmitted lymph has certain advantages over long humanized virus; these may be stated as follows:

1. Animal vaccination produces a vaccinia which approaches more nearly the Jennerian prototype, and reaches therefore a greater degree

of perfection than that produced by long humanized virus. The cow-pox casually produced on the hands of dairymaids was believed by Jenner to confer full and complete protection against smallpox. The bovine species appears to be the natural soil of the prophylactic pock, and the view is maintained by many that bovine lymph, or that derived from an early human remove, creates a more complete and more lasting immunity. The inferiority of humanized virus is doubtless due to a weakening or degeneration of the lymph product as a result of the long-continued transmission through the human subject. Jenner really anticipated such a deterioration in the quality of vaccine lymph from this cause. Copeman says that "in the present state of our knowledge, however, such enfeeblement of the specific virus can hardly be regarded as probable, except under conditions that may be obviated by reasonable skill and care on the part of the operator. Jenner early discovered that vaccine lymph only exhibited its full degree of activity when taken at the stage of maturation of the vesicle, and before its contents became at all purulent. If this precaution be observed, together with strict cleanliness in the removal and insertion of the lymph, experience has shown that no appreciable degeneration can be demonstrated."

2. The use of animal lymph precludes the possibility of transmitting by vaccination diseases peculiar to the human species. One of the most weighty reasons that led to the adoption of animal vaccination and to its preference over arm-to-arm transmission was the recognition of the possibility of inducing syphilis by vaccine inoculation. No matter how rare such an accident might be, the remotest liability of such an occurrence constitutes a serious argument against the use of humanized lymph. The bovine species being totally insusceptible to syphilis, lymph derived from this source is incapable of transmitting such infection.

Erysipelas appears to be a much rarer complication of vaccinia since the general employment of animal lymph. It is probable that many cases of vaccinal erysipelas in the past were due to secondary infection of the vesicle at the time that it was punctured to withdraw lymph for further inoculations. The almost universal use of animal lymph removes the necessity of tapping the vaccine vesicle, thus rendering erysipelas from this cause practically non-existent. Again, many cases of erysipelas were doubtless the result of the employment of crusts which had not been wisely selected or properly preserved. Whatever the cause or causes may have been, actual experience shows an enormous reduction in the relative and aggregate incidence of this complication since vaccination with humanized lymph has fallen into desuetude.

There is little or no danger of transmitting tuberculosis in bovine lymph, inasmuch as, in addition to the diagnostic use of tuberculin, all calves are killed and carefully examined in well-regulated establishments before the virus is sent out; furthermore, it has been shown that the admixture of glycerin to the lymph is capable of destroying the life of any tubercle bacilli that may be present.

3. Animal vaccination offers an almost inexhaustible supply of vac-

cine lymph, for the number of calves yielding the same can be multiplied at will. During extensive epidemics of smallpox, when human vaccine was employed, the community was often placed in an embarrassing and dangerous predicament owing to an insufficient supply of vaccine material. During the great pandemic of smallpox from 1870 to 1873, a veritable vaccine famine existed in many countries. All sorts of vaccinifers were drawn upon, and much worthless lymph derived from spurious and irregular cases was employed, of course, with entirely unsatisfactory results.

4. Animal lymph appears to give a much larger percentage of successful revaccinations than long humanized virus. Martin says: "The number of those who, in revaccination with the old, long humanized virus (not that of early human removes) experience vaccinal effect may be stated at the outside at 35 per cent. The number of those revaccinated with equal care and repetition with animal virus and virus of very early human removes, I affirm to be a fraction over 80 per cent.—a difference of 45 per cent.; and this 45 per cent. I firmly believe to approximately represent the number of those insensible to the enfeebled influence of long humanized virus, but sensible to the intense contagium of variola just in the same degree as sensible to the intense power of bovine virus and that of the early human removes from it."

Comparison of the Course of Vaccinia Produced by Original Cowpox Virus, Long Humanized Virus, and Calf-transmitted Virus, Respectively. Original Cowpox Virus.—The vaccine disease produced by virus from a case of *original cowpox* or from early human removes therefrom lasts from twenty-one to thirty-two days, counting from the insertion of the lymph to the falling of the crust. At the end of the third or beginning of the fourth day papulation occurs; vesiculation takes place at the end of the fifth day, but the vesicle continues to grow until the decline of the areola or even a few days after this. The vesicle has a pearly or slightly bluish tint; it really resembles, as Jenner remarked, "a section of a pearl on a rose-leaf." The areola appears first about the end of the ninth or beginning of the tenth day and persists until the twelfth, thirteenth, or fourteenth day. Desiccation and formation of the crust are not complete before the sixteenth or seventeenth day; the crust is never spontaneously detached before the twenty-first day and usually not before the twenty-fifth to the twenty-eighth day. Occasionally it will remain upon the vaccine site until the thirtieth or thirty-second day. The crust is round, thick, umbilicated, and of a rich brown or mahogany tint.

A very decided febrile reaction attends the rise, development, and decline of the areola. This febrile disturbance was considered to be of great importance by the early vaccinators, especially Jenner, who regarded it as a *sine qua non* of vaccinal impression upon the system, and an indelible characteristic cicatrix remains after the termination of the disease. In the early days it was not at all rare for the vesicle to break down and ulcerate, leading to a spreading and troublesome loss of tissue and occasionally to erysipelatous infection.

Long Humanized Virus.—The most distinguishing characteristic of the vaccinia produced by long humanized virus is the brevity of the course of the disease. The duration varies very much with different lymph stocks. With a virus used by Martin and obtained from Ceely, the course of the disease from the time of insertion of the lymph to the spontaneous detachment of the crust was but eleven days; whereas with a lymph of French origin employed by Martin, the crust came off from the twenty-first to the twenty-sixth day. Lymph from the National Vaccine Institution of Great Britain ran a course of fourteen days to the falling of the crust. These various "stocks," although propagated for years, preserved their distinctive durations. It was even found, when two different lymphs were inserted—one on one arm and the second on the other—that each strain retained its special features.

In brief, it may be stated that long humanized lymph produces a vaccinia of shorter duration and milder intensity than original and early virus. With the lymph which induced a vaccinia of eleven days' duration, the areola was formed on the seventh day and sometimes on the sixth. The Jennerian "stock" of the British Vaccine Institution induced a vaccina of fourteen days' duration, the areola developing on the seventh or eighth day.

The crust derived from vaccination with long humanized lymph is very small, thin, and often devoid of umbilication. The febrile reaction accompanying such a vaccinia is slight or absent, even when many insertions are made.

Calf-transmitted Virus.—As would be expected the vaccinia resulting from the employment of calf-transmitted lymph closely resembles the disease induced by early human removes from original cowpox, such as were observed by Jenner. With the animal-transmitted virus, however, the reaction is not so violently inflammatory as that which occurred with original cowpox lymph. Ceely, in 1840, stated his belief that the tendency to undesirable intensity in the original cowpox is tempered by successive transmissions through young animals. He inoculated a series of eleven calves and found that the objectionable qualities of the lymph, as determined by human vaccinations, were gradually but progressively eliminated. The animal virus now used usually runs its course from twenty-one to thirty days.

Glycerinated Lymph.—To S. Monckton Copeman¹ belongs the credit of advocating the addition of glycerin as a vaccine purifier, and of establishing the employment of glycerinated lymph upon a scientific basis. Glycerin had previously been used for the purpose of increasing the volume of the lymph and also as a lymph preservative.

As far back as March, 1850, Mr. R. Cheyne² advocated (in a letter appearing in the *Medical Times*) the use of fluid lymph to which some glycerin had been added as superior to the dry points. In 1853 he

¹ We desire to acknowledge our indebtedness for much of the material presented in this chapter to the admirable book of S. Monckton Copeman (*Vaccination, its Natural History and Pathology*, London, 1899), which we have freely consulted.

² Copeman appears to have been unaware of Cheyne's work until a few years ago.

demonstrated to the presidents of the Royal Colleges of Physicians and Surgeons a child whom he had successfully vaccinated with glycerinated lymph prepared six months previously. Cheyne admitted that he was indebted for knowledge of this procedure to the previous publications of Mr. J. Startin on the *therapeutic uses of glycerin*.

Müller, of Berlin, further demonstrated the fact that vaccine lymph could be considerably increased in quantity by the admixture of glycerin without interfering with its specific activity. He proved that the lymph might be diluted with three times its bulk of glycerin without in any way lessening its potency. It is evident that Müller's chief object was to increase the quantity of available lymph, a matter of much importance during smallpox epidemics, particularly when there was danger of a vaccine famine.

With the same object in view Dr. Stephen Mackenzie, of the London Hospital, during the great smallpox epidemic in 1870-71, added glycerin to lymph in order to increase the amount just before conducting a large series of vaccinations.

Dr. Warlomont, of Brussels, in 1882 placed upon the market, under English patent, a method of admixture of glycerin with vaccine lymph, but no mention was made of the contained glycerin until some years later.

Copeman, in a paper presented to the International Congress of Hygiene, held in London in 1891, advocated the addition of glycerin to vaccine lymph for the purpose of purifying and preserving it. The method consisted in the "intimate admixture of a given amount of lymph, or rather vesicle pulp, with a sterilized 50 per cent. solution of chemically pure glycerin in distilled water, and in subsequent storage of the resultant emulsion in sealed capillary tubes for several weeks."

Copeman had previously endeavored by diverse means to inhibit the growth in vaccine material of the various extraneous organisms, and if possible destroy them without weakening the specific activity of the lymph. These measures failing, he resorted to the addition of glycerin.

Previous to Copeman's experiments there had been no appreciation of the influence of the glycerin as a bacteriological purifier of lymph when the mixture is stored for some time and protected from the access of light and air.

When a glycerin emulsion of vaccine is prepared in the manner indicated by Copeman, an inhibition and later destruction of the foreign aërobic bacteria is brought about. The purification is a gradual one, as can be determined by making plate cultures of the lymph from time to time, and estimating the number of colonies of organisms present.

Since the publication of Copeman's paper in 1891, other careful observers have fully substantiated the claims of this investigator. Chambon and Ménard, in 1892, were not only able to purify and preserve lymph by glycerin admixture, but they claim to have produced an improvement in the activity of lymph which in its fresh state had given only mediocre results. Such a lymph produced after fifteen days'

admixture with glycerin a passable vesicle, and after forty, fifty, or sixty days a typical one. The improvement in potency was attributed by them to the gradual destruction of foreign bacteria in the fluid. Professor Straus, who made plate cultures of this lymph, achieved results identical with those obtained by Copeman, although the work was done prior to the publication of Copeman's article. Fresh glycerinated lymph gave rise to numerous colonies of various organisms, especially the staphylococcus pyogenes aureus and staphylococcus albus, but when stored for fifty to sixty days plate cultures proved to be absolutely sterile as regards these extraneous bacteria. These experiments were repeated many times, but always with the same result.

Leoni, in a paper read before the International Medical Congress, held in Rome in 1894, concludes that (1) recently collected vaccine is a contaminated vaccine, containing numerous foreign germs, some of which are capable of exerting pathogenic properties when inoculated into the system; (2) the contaminating organisms become extinguished in vaccine preserved for a certain period in glycerin; (3) vaccine preserved in glycerin from one to four months after it is collected is the type of *pure* vaccine, with an *exclusively specific virulence*; (4) this is the quality of vaccine with which the hygienist of to-day should concern himself in the prophylaxis of variola.

Klein has added the weight of his testimony as to the purifying influence of glycerin on vaccine lymph. In stating his belief that the specific organism of variola is probably a spore-bearing bacillus, he incidentally remarks: ". . . it is established that the active principle of vaccine is preserved in glycerin, although, as is also known, glycerin is a germicide for cocci and sporeless bacilli."

In 1896 the German government appointed a commission presided over by Schmidtman, and including Koch, Pfeiffer, and Frosch, together with the Directors of the Vaccine Institutes of Berlin, Cologne, and Stettin, to investigate into the best methods for the collection, preservation, storage, distribution, and use of vaccine lymph. The report stated that fresh lymph contained numerous bacteria which diminish progressively under the influence of the glycerin admixture. Streptococci and diphtheria organisms added to the lymph were killed in eleven days and twenty days, respectively. These experimenters, as well as Kitasato, in Japan, determined that glycerin with distilled water could be added to the extent of from fifteen to twenty times the weight of vesicle pulp without destroying the vaccine principle.

Copeman and Blaxall have shown that not only are the ordinary foreign bacteria of fresh lymph destroyed by glycerinization, but that pathogenic organisms such as those of tuberculosis and erysipelas, when added in large number for experimental purposes, also perish.

The fact that the tubercle bacillus thrives particularly well upon agar containing 6 per cent. of glycerin does not invalidate the claim that this agent in a strength of 40 to 50 per cent. is a valuable microbicide. Indeed, Copeman and Blaxall and likewise Klein have proven that tubercle bacilli cannot be recovered after exposure for a month to the

action of glycerin, present to the extent of about 40 per cent., either in a culture in sterile bouillon or in fresh vaccine material. These investigators have furthermore shown that an emulsion of glycerinated lymph inoculated with active tubercle bacilli, and allowed to stand for a month, was incapable of producing tuberculosis in guinea-pigs, whereas the contaminated vaccine lymph without the glycerin added invariably produced this disease.

Rosenau¹ (1903), in a study of the germicidal action of glycerin, concluded that it has distinct but very feeble germicidal and antiseptic properties.

Small quantities of glycerin, less than 10 per cent., added to nutrient media, have well-known powers of favoring the growth and multiplication of many forms of bacteria.

The presence of 50 per cent. of glycerin will restrain all bacterial growth. No growth or multiplication of bacteria takes place in nutrient media containing 32 per cent. of glycerin, but moulds grow in stronger percentages, viz., 40 to 49 per cent.

In order to prevent the growth and development of pus cocci, at least 33 per cent. of glycerin must be present.

The germicidal action of glycerin is probably due to its affinity for water, causing a dehydration of the bacteria.

Glycerin ordinarily destroys the micrococci of suppuration, whether these be in pure culture or in the pus itself, within two weeks. This action varies according to the temperature. Pus cocci may live in glycerin for months in the ice-chest, whereas at the body temperature they die in a week.

Glycerin has a selective influence upon the diphtheria bacillus, which succumbs much more quickly than most other organisms.

The bacteria of the typhoid and colon group often show a marked resistance to the effects of glycerin in strong proportions.

Glycerin in all strengths has practically no effect upon endogenous spores. Anthrax spores were kept alive and virulent two hundred days in the strongest percentages of glycerin, and at warm temperatures.

Tetanus spores in pure culture, freed of all organic matter and washed free of toxin, may lose their virulence in glycerin in thirty days at the body temperature, but they live for months (one hundred and eighty days) at room temperature or in the ice-chest. Glycerin, therefore, cannot be depended upon to purify vaccine or other organic matter containing this contamination. The virulence of the spores is lost long before they actually die, for they still retain the power of growing and multiplying if placed under favorable conditions.

Under these circumstances, therefore, they also regain their original pathogenoid properties. Glycerin has practically no effect on diphtheria toxin.

At a meeting of the British Medical Association in 1896, Copeman and Blaxall presented a paper on "The Influence of Glycerin upon the

¹ Director of the Hygienic Laboratory, United States Public Health and Marine Hospital Service, Bulletin 16, 1903.

Growth of Bacteria." The bacteria employed in the experimentations comprised staphylococcus pyogenes aureus, staphylococcus pyogenes albus, streptococcus pyogenes, bacillus pyocyaneus, bacillus subtilis, bacillus coli communis, bacillus diphtheriæ, and bacillus tuberculosis. Smallpox and vaccine material in the form of "crusts" and lymph were also employed.

"Results: 1. No visible development of the micro-organisms employed took place in the presence of more than 30 per cent. of glycerin.

"2. None of the micro-organisms experimented with could be recovered after exposure for a month to the action of from 30 to 40 per cent. glycerin, with the exception of bacillus coli communis and bacillus subtilis when kept in the cold.

"3. Bacillus coli communis, unlike bacillus typhosus, resists the action of 50 per cent. glycerin in the cold for a considerable period—a fact likely to prove of value as an addition to our present methods of differentiating these microbes one from another.

"4. The samples of smallpox and vaccine material, whether as 'crusts' or lymph, were sterilized completely, so far as extraneous microbes were concerned, in a week, by the presence of glycerin to the extent of about 40 per cent. in the broth tubes. This short period of resistance is, doubtless, in part to be explained by the fact that the smallpox crusts used in these experiments had been obtained several months beforehand. Presumably, therefore, the number of microbes which had been able to survive for so long a period the process of drying would be much less than might be expected to be present in 'crusts' recently obtained."

Copeman sets forth the advantages of glycerinated lymph in the following terms:

"1. By employing the method of glycerination of lymph pulp, great increase in quantity can be obtained without any consequent deterioration in quality, the percentage of insertion success following on its use being equal to that obtained with perfectly active fresh lymph.

"2. Glycerinated lymph does not dry up rapidly as does unglycerinated lymph, thus simplifying the process of vaccination.

"3. Glycerinated lymph does not coagulate; so that it never becomes necessary to discard a tube on this account.

"4. *Glycerinated lymph can be produced absolutely free from the various streptococci and staphylococci* which are usually to be found in untreated calf lymph, and which are, under certain circumstances, liable to occasion suppuration.

"5. In like manner the streptococcus of erysipelas, in the event of its having been originally present in the lymph material, is rapidly killed out by the germicidal action of the glycerin.

"6. The tubercle bacillus is effectually destroyed even when large quantities of virulent cultures have been purposely added to the lymph.

"7. The possibility of inoculation of syphilis is eliminated, as the calf is not subject to this disease.

"8. The necessity for collecting children together, with the attendant

risk of spread of infectious diseases, or of transporting a calf from place to place, is obviated, while the danger of 'late' erysipelas in the child is diminished by reason of there being no necessity to open the mature vesicles for the purpose of obtaining lymph.

"9. The bacteriological purity and clinical activity of large quantities of the lymph can be readily tested prior to distribution.

"10. By reason of the possibility of keeping large stocks of glycerinated lymph on hand for considerable periods of time without appreciable deterioration, any sudden demand, such as is likely to arise on the outbreak of epidemic smallpox, can be promptly met.

"11. The expense of producing glycerinated lymph is proportionately small, since the amount obtainable from each calf is enormously increased."

Rosenau¹ made a study of the bacteriological impurities of vaccine virus as it occurs in commercial preparations upon the market in the United States. The virus of ten different vaccine propagators was examined during a period of more than a year. Of 190 dry points examined, an average of 4354 bacteria per point was found. A number of the points contained over 15,000 and one as high as 44,000 organisms.

Of 244 tubes of glycerinated virus examined, an average of 1742 bacteria per tube was found. A number of the capillary tubes contained over 10,000 bacteria, and one as high as 30,000. This evidenced lack of care in the preparation of the lymph.

Pus cocci, pathogenic for laboratory animals, were found both in dry points and the glycerinated virus. Much of the virus above referred to was "green"—*i. e.*, it had not been glycerinated for a sufficient period.

During the winter of 1901-02 the glycerinated virus contained an average of 4698 bacteria per tube. In the spring of 1902 the average fell to 1058 bacteria per tube. In the winter of 1902, 89 tubes examined gave an average of 29 bacteria per tube; the maximum was 239.

Glycerinated virus when properly prepared is freer from impurities than dry points made with fresh lymph.

There is practically no difference between the glycerinated virus dried upon ivory points and that hermetically sealed in capillary tubes, so far as bacteriological impurities are concerned.

Tetanus spores may live a long time in vaccine virus; they remained alive and virulent on dry points after two hundred and ninety-five days, and in glycerinated virus sealed in capillary tubes three hundred and fifty days.

Rosenau was unable to find tetanus germs or spores in any of the considerable number of glycerinated points and tubes examined with this object in view. He states that tetanus organisms cannot grow or produce their toxin either in glycerinated virus or on the dry points. "It would take gross carelessness to contaminate the vaccine with a sufficient number of tetanus spores to carry the disease to those vaccinated."

The writer concludes that the excessive impurities found in some of the glycerinated virus upon the market is largely due to the overconfidence in the germicidal value of glycerin.

Vaccine propagators become careless, trusting to the glycerin to purify the product. Glycerin is too feeble a germicide to purify vaccine matter which has a great initial contamination.

The virus is also at times put upon the market with undue haste when an unusual demand exists.

Howard¹ found actinomyces in virus from five vaccine establishments twenty-four times in a total of ninety-five cultures. Nine different species of actinomyces were found, of which six appeared to be previously undescribed. The organisms are supposed to reach the virus from the air, water, soil, hay, straw, and hide.

The writer thinks it is not improbable that some of the postvaccinal suppuration infections are caused by these organisms and are cases of atypical actinomycosis.

Sabrazis, and Jolly and Folli, also found actinomyces in vaccine virus.

The Preparation of Glycerinated Calf Lymph (Copeman).—"The method best adapted for the production of glycerinated calf lymph which shall be free from all extraneous organisms, of perfect efficacy, and yet affording material for the vaccination of many more children than the original unglycerinated calf lymph, is briefly as follows:

"**THE PREPARATION OF THE CALF.**—A female calf of suitable age, about from three to six months, should be kept under observation for a week, after which, if found to be quite healthy, it may be removed to the vaccination station. It is there placed on a tilting table, and the lower part of the abdomen, reaching as far forward as the umbilicus, is shaved and thoroughly washed with a solution of carbolic acid and then rinsed with sterile water and dried with soft, sterilized towels.

"**INOCULATION OF THE CALF.**—With a sterilized, sharp scalpel incisions about four inches long and half an inch apart, parallel to the long axis of the body, are made on this clean-shaven area. The depth of the incision should be such as to pass through the epidermis and to open the rete Malpighii, if possible without drawing blood. As these incisions are made, glycerinated calf lymph, which by examination has been proved to be free from extraneous organisms, is run into them by means of a sterilized blunt instrument, and the point of the scalpel is from time to time dipped into the vaccine emulsion.

"**COLLECTION FROM THE CALF.**—After five days (one hundred and twenty hours) the vaccinated surface of the calf is first thoroughly washed with warm water and soap, rubbed over it by the clean hand of the operator, and finally the whole area is carefully cleansed with sterile water. The remaining moisture is then removed by sterilized sheets of blotting paper. The vaccinated incisions will now appear as lines of continuous vesicles raised above the surface, each line separated from its neighbor by about a quarter of an inch of clear skin. Any crusts which appear

¹ A Study of Actinomyces Cultivated from Commercial Vaccine Virus, Journal of Medical Research, January, 1904.

in the vesicular lines are picked off with a blunt, sterilized instrument. The vesicles and their contents are then removed by means of a sterilized Volkmann spoon, and transferred to a sterilized bottle of known weight. By going over the lines only once with the spoon, it is quite easy to remove the whole of the pulp without any admixture of blood. The abraded surface is carefully washed, and may be dusted over with fine oatmeal or starch and boracic powder. Subsequently, the calf is transferred to the slaughter house and the carcass is examined by the veterinary surgeon, who forwards a certificate of its condition. Should this not be satisfactory, the vaccine pulp obtained from the animal is destroyed.

FIG. 16



Belly of heifer, showing one of the approved modern methods of propagating vaccine virus; lesion^a photographed at the end of five days. (Courtesy of Mr. Wm. F. Elgin.)

"PREPARATION AND GLYCERINATION OF THE LYMPH PULP.—The bottle containing the vaccine pulp is taken to the laboratory and the exact weight of the material ascertained. A calf vaccinated in this way will yield from 18 to 24 grams, or even more, of lymph pulp. This material is then thoroughly rubbed up in a sterilized mortar or in a mechanical triturating machine. When it has been brought to a fine state of division, it is mixed with six times its weight of a sterilized solution of 50 per cent. chemically pure glycerin in distilled water. The resulting emulsion is then transferred to small test-tubes, which are then aseptically sealed and should be stored in a cool place protected from light. When required for distribution it is drawn up into sterilized capillary tubes, which are subsequently sealed in the flame of a spirit lamp.

'BACTERIOLOGICAL EXAMINATION OF THE LYMPH EMULSION.—As soon as the vesicular pulp is thoroughly emulsified with the glycerin solution, agar-agar plates are established from it, and, after suitable incubation for seven days, the colonies that have developed on the plates are counted and examined. Week by week this process is repeated, and invariably the number of colonies diminishes with the age of the emulsion, until at the end of the fourth week after the collection and glycerination of the lymph material the agar-agar plates inoculated at that time show no development of colonies. The lymph is then subjected to further culture experiments, and if these results of freedom from extraneous organisms are confirmed the emulsion is ready for distribution. The elimination of the extraneous organisms in our experiments has occurred with marked regularity at the end of the fourth week. The only exception to this rule arises when the lymph originally contained a considerable number of spores or bacilli of the hay bacillus or bacillus mesentericus. These organisms are very resistant to the action of glycerin, but if the precautions detailed are carried out in the treatment of the calf their presence may generally be excluded.

"DURATION OF ACTIVITY OF GLYCERINATED CALF LYMPH.—This varies in all probability with atmospheric conditions, with the fineness of division of the vesicle pulp, and, above all, with the condition of the calf itself. Some calves yield an excellent lymph, others a poor lymph, and the problem is to determine the value of the lymph yielded by any given calf. A lymph which was collected and glycerinated on July 13, 1897, has since been used at intervals of from twenty-four weeks to thirty-two weeks after glycerination for the vaccination of children. During this period sixty-one children have been vaccinated with this lymph in five places each, with a mean insertion success of 98 per cent. Thus, by the methods described, glycerinated calf lymph can be prepared which becomes freed from extraneous organisms, is available for a large number of vaccinations, at least 5000 from an average calf, and retains full activity for eight months, and will, under favorable circumstances continue to do so in all probability for still longer periods, if necessary."

STATISTICAL EVIDENCE OF THE EFFICACY OF VACCINATION.

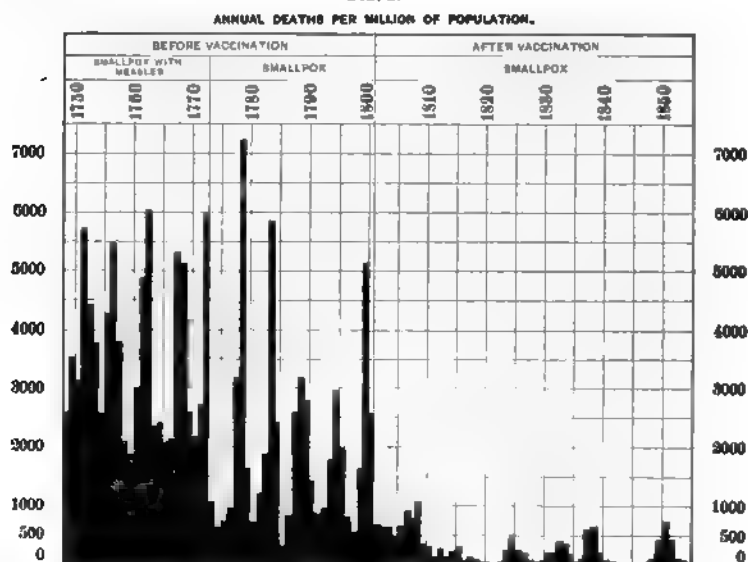
Although smallpox dates back many centuries, we have no trustworthy record of the extent of its prevalence before the fifteenth century. About this time it began to be common in Western Europe, increasing during the sixteenth and particularly the seventeenth century, and prevailing still more extensively in the eighteenth.

The beginning of the nineteenth century was characterized by a sudden and striking decrease in the morbidity and mortality of smallpox.

Inasmuch as the announcement of the protective influence of vaccination (1798) and the diffusion of this practice immediately preceded this decline, there is the strongest reason to regard Jenner's epoch-making discovery as the causative influence.

As has been previously shown, smallpox was a great scourge before the days of vaccination. But a small percentage of the population escaped its ravages. It is claimed that in the eighteenth century, according to contemporaneous writers, 95 per cent. of the inhabitants of European countries suffered at one time or other from the smallpox. In other words, but five persons out of every hundred went through life without being attacked by this dread malady. This is rendered credible when we appreciate the fact that smallpox is among the most contagious of all diseases, and that nearly every human being is highly susceptible to it. Haygarth, who lived in the eighteenth century, stated that the proportion of mankind incapable of infection by smallpox "was observed to amount to one in twenty;" this would account for the exemption of the 5 per cent. referred to.

FIG. 17



Smallpox death rates for Sweden from 1749 to 1855. (Calculated by Mr. Haile from returns communicated by the Swedish government. Published in papers communicated to the Houses of Parliament, London, 1857.)

This author reports an epidemic of smallpox in Chester in 1774, at which time, out of a population of 14,713, 1202 persons took the disease and 202 died. At the termination of the epidemic there were but 1060 persons, or 7 per cent., of the population who had never had smallpox.

In an epidemic of smallpox at Warrington in 1773, in a population of 8000, 211 persons succumbed to the disease. The total deaths during the year from all causes were 473.

In 1722 an epidemic raged in the small English town of Ware, which had a population of 2515. Of this number there were only 914 persons susceptible to smallpox, as 1601 had already had the disease. During the epidemic 612 persons were attacked, leaving but 302 individuals in the entire town who had never had smallpox.

Rapid Decline in Smallpox Mortality After the Introduction of Vaccination.—Inasmuch as accurate records of smallpox mortality were kept in various countries, it is possible to prove by documentary evidence that a striking fall in the number of deaths from this disease occurred shortly after the introduction of vaccination.

Sweden.—Vaccination was introduced into this country in October, 1801. According to the official figures of the Medical College, there were performed 25,000 vaccinations by the year 1805, 23,000 in 1805, and about 19,000 in 1806. Vaccination was made compulsory in 1816. The average death rates per million of population for the decades from 1774 to 1821 show a decided and progressive decrease in the mortality of smallpox. (See Fig. 17.)

AVERAGE YEARLY DEATH RATES FROM SMALLPOX PER MILLION OF POPULATION FOR DECADES FROM 1774 TO 1821. SWEDEN.

(Eight years), 1774 to 1781 (before vaccination)	1999
Decade, 1782 " 1791 " "	2219
" 1792 " 1801 " "	1914
" 1802 " 1811 (after vaccination)	623
" 1812 " 1821 " "	133

The influence of vaccination in lessening smallpox mortality in Sweden is so clearly shown in the above table as to require no further discussion.

The contrast in smallpox mortality may be expressed in another manner. In the *twenty-eight years before vaccination* in Sweden, there died each year from smallpox, out of each million of population, 2050 persons; during the *forty years following vaccination*, out of each million of population the smallpox deaths annually averaged 158.

The official figures of the Medical Faculty of the University of Prague (published in papers on vaccination issued by the London Board of Health, 1857) are no less conclusive:

POPULATION, TOTAL DEATHS, AND DEATHS BY SMALLPOX DURING SEVEN YEARS BEFORE THE GENERAL INTRODUCTION OF VACCINATION. PRAGUE.

Year.	Population.	Deaths.		Remarks.
		Total number.	From smallpox.	
1796	3,003,482	92,242	6,686	{ The proportion of the deaths generally to population = 1 : 32.
1797	2,991,846	86,855	1,988	
1798	3,045,926	84,743	3,105	
1799	3,041,608	99,079	17,587	{ Deaths from smallpox to populations 1 : 396 ² / ₃ .
1800	3,047,740	110,730	17,077	
1801	3,036,481	105,576	3,169	{ Deaths from smallpox to the total number of deaths = 1 : 12 ¹ / ₃ .
1802	3,111,472	85,460	4,029	
Total	21,278,055	664,685	53,641	
Average	3,039,722 ¹ / ₇	94,955	7,663	

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DURING TWENTY-FOUR YEARS SUBSEQUENT TO INTRODUCTION OF
VACCINATION. PRAGUE.

Year.	Population	Deaths.		Remarks.
		Total number.	From smallpox.	
1882	3,888,628	139,061	907	The proportion of the total number of deaths to population = 1 : 32%.
1883		121,679	583	
1884		122,171	255	
1885		122,952	337	
1886	3,945,875	124,015	291	Deaths from smallpox to population = 1 : 14,741%.
1887		141,982	104	
1888		106,419	62	
1889		121,400	128	
1890	4,027,581	118,471	699	Deaths from smallpox to total number of deaths = 1 : 457%.
1891		116,575	697	
1892		124,019	539	
1893		142,876	332	
1894	4,285,780	118,184	150	
1895		178,826	62	
1896		132,379	59	
1897		134,490	9	
1898	4,480,661	141,408	115	
1899		181,493	383	
1900		176,211	478	
1901		183,245	508	
1902	4,613,080	184,921	348	
1903		124,617	42	
1904		124,746	68	
1905		124,764	64	
Total	33,985,240	3,153,905	6895	
Average	4,248,155	131,412 ^{71/24}	287 ^{11/24}	

TABLES COMPARING SMALLPOX MORTALITY IN VARIOUS LOCALITIES BEFORE AND AFTER THE INTRODUCTION OF VACCINATION.

Terms of years respecting which particulars are given.		Territory	Approximate average. Annual death rate by smallpox per million of living population.	
Before vaccination.	After vaccination.		Before introduction of vaccination.	After introduction of vaccination.
1777-1806 and 1807-1850		Austria, Lower	2,484	240
1777-1806	1807-1850	Austria, Upper, and Salzburg	1,421	501
1777-1806	1807-1850	Styria	1,052	446
1777-1806	1807-1850	Illyria	518	244
1777-1806	1807-1850	Trieste	14,046	182
1777-1803	1807-1850	Tyrol and Vorarlberg	911	170
1777-1806	1807-1850	Bohemia	2,174	215
1777-1806	1807-1850	Moravia	5,402	255
1777-1806	1807-1850	Silesia (Austrian)	5,812	198
1777-1806	1807-1850	Gallicia	1,194	678
1787-1806	1807-1850	Bukowina	3,527	616
	1817-1850	Dalmatia	85
	1817-1850	Lombardy	87
	1817-1850	Venice	70
	1831-1850	Military Frontier	285
1776-1780	1810-1850	Prussia (East Province)	3,321	536
1780	1810-1850	Prussia (West Province)	2,272	356
1780	1816-1850	Posen	1,911	743
1776-1780	1810-1850	Brandenburg	2,181	181
1776-1780	1816-1850	Westphalia	2,643	114
1776-1780	1816-1850	Rhenish Provinces	908	80
1781-1805	1810-1850	Berlin	3,422	176
1776-1780	1816-1850	Saxony (Prussian)	719	170
1780	1810-1850	Pomerania	1,774	120
1774-1801	1810-1850	Silesia (Prussian)	319
1761-1800	1801-1850	Sweden	2,060	158
		Copenhagen	3,128	226

It will be seen from the above tables that whereas in the seven years preceding the introduction of vaccination smallpox in Prague caused *one-twelfth of the total number of deaths*, this disease during twenty years of the vaccination period caused but $\frac{1}{457}$ of the total number of deaths.

In Westphalia the annual deaths from smallpox from 1776 to 1780 were 2643 *per million* of population; during the thirty-five years from 1816 to 1850 the *death rate was only* 114 per million.

In Copenhagen, for the half-century 1751 to 1800, the smallpox death rate was 3128, whereas for the next fifty years it was only 286.

In Berlin for twenty-four years preceding vaccination the death rate from smallpox was 3422, and for the first forty years of the vaccination era it was 176.

By the middle of the nineteenth century the fatality of smallpox had been reduced in Copenhagen to one-eleventh of the prevaccination death rate; in Sweden to a little over a thirteenth; in Berlin, and in a large part of Austria, a twentieth; and in Westphalia, a twenty-fifth. In the last-named place but four persons died about the middle of the century compared to 100 in the prevaccination days.

SMALLPOX DEATHS EACH YEAR, FROM THE "BILLS OF MORTALITY,"
London, 1801 TO 1830.

Before vaccination era.				After vaccination era.			
Decade.		Smallpox deaths.		Decade.		Smallpox deaths.	
1761-1770		20,434		1801-1810		12,534	
1771-1780		20,923		1811-1820		7,858	
1781-1790		17,867		1821-1830		6,990	
1791-1800		18,477					
1801-1810		1811-1820		1821-1830		1831-1837	
1801 . . . 1,461		1811 . . . 751		1821 . . . 508		1831 . . . 563	
1802 . . . 1,597		1812 . . . 1287		1822 . . . 604		1832 . . . 771	
1803 . . . 1,202		1813 . . . 898		1823 . . . 774		1833 . . . 574	
1804 . . . 622		1814 . . . 638		1824 . . . 725		1834 . . . 334	
1805 . . . 1,685		1815 . . . 725		1825 . . . 1299		1835 . . . 863	
1806 . . . 1,158		1816 . . . 653		1826 . . . 503		1836 . . . 536	
1807 . . . 1,279		1817 . . . 1051		1827 . . . 616		1837 . . . 217	
1808 . . . 1,169		1818 . . . 421		1828 . . . 598			
1809 . . . 1,163		1819 . . . 712		1829 . . . 736			
1810 . . . 1,198		1820 . . . 722		1830 . . . 627			
<hr/> Smallpox, 12,534		<hr/> 7856		<hr/> 6990		<hr/> 3858	

The above figures show a decided contrast in smallpox mortality between the decades immediately preceding and following the introduction of vaccination. In the twenty-seven years elapsing from 1811 to 1837 the smallpox deaths exceeded 1000 but three times.

Berlin.—Below are compared the deaths from smallpox *per* 100,000 inhabitants in the prevaccination and postvaccination periods:

1758-1762 . . . 407 persons.	1790-1794 . . . 310 persons.
1763-1767 . . . 364 "	1795-1799 . . . 239 "
1768-1772 . . . 294 "	1800-1804 . . . 261 "
1773-1784 . . . ? "	1805-1809 . . . 308 "
1785-1789 . . . 360 "	

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(In the first decade of the nineteenth century vaccination was not actively practised in Berlin; it became generally employed in the year 1810.)

1810-1814	. . .	31 persons.	1840-1844	. . .	13 persons.
1815-1819	. . .	40 "	1845-1849	. . .	2 "
1820-1824	. . .	4 "	1850-1854	. . .	5 "
1825-1829	. . .	13 "	1855-1859	. . .	18 "
1830-1834	. . .	19 "	1860-1864	. . .	30 "
1835-1839	. . .	18 "	1865-1869	. . .	26 "

In the quinquennium 1870-1874 occurred the great pandemic of smallpox which swept the entire civilized world. There died in Berlin during this period, per 100,000 population, a yearly average of 160; this number considerably exceeds all the previous years of this period, but still falls far below the average of the prevaccination years.

From 1795 to 1799, before the days of vaccination, smallpox caused 6.5 per cent. of all deaths in Berlin. In the five years following the introduction of vaccination the figures were: 7.5 per cent., 6.4 per cent., 0.7 per cent., 1.3 per cent., and 0.2 per cent.¹

Copenhagen.—Between 1794-1798 (prevaccination period) smallpox caused on an average 373 deaths each year.

1799 (before vaccination)	. .	54	1805 (after vaccination)	. .	5
1800 "	" "	35	1806 "	" "	5
1801 "	" "	486	1807 "	" "	2
1802 "	" "	73	1808 "	" "	46
1803 (after vaccination)	. .	5	1809 "	" "	5
1804 "	" "	13	1810 "	" "	4

*From 1811 to 1823 not a death occurred from smallpox. (A period of thirteen years.)*²

It is thus seen from the statistics above quoted that after the discovery of vaccination the deaths from smallpox markedly decreased in every country in which this practice was introduced.

¹ Denkschrift, k. k. Gesundheitsamt, Berlin.
² Beiträge aus der Gesundheitsamte. Quoted by Edwardes, Smallpox and Vaccination in Europe, London, 1902.

ACTUAL SMALLPOX DEATHS IN SWEDEN BEFORE AND AFTER THE
INTRODUCTION OF VACCINATION.

Some deaths from measles included.	1749 (before vaccination)	4,458	1802 (after vaccination)	1,533	
	1750 "	6,180	1803 "	1,464	
	1751 "	5,546	1804 "	1,460	
	1752 "	10,302	1805 "	1,090	
	1753 "	8,000	1806 "	1,482	
	1754 "	6,862	1807 "	2,129	
	1755 "	4,705	1808 "	1,814	
	1756 "	7,858	1809 "	2,404	
	1757 "	10,241	1810 "	824	
	1758 "	7,104	1811 "	689	
	1759 "	3,910	1812 "	404	
	1760 "	3,568	1813 "	547	
	1761 "	5,731	1814 "	308	
	1762 "	9,389	1815 "	472	
	1763 "	11,662	1816 "	690	
	1764 "	4,562	1817 (compulsory vaccination)	242	
	1765 "	4,697	1818 "	305	
	1766 "	4,092	1819 "	161	
	1767 "	4,189	1820 "	143	
	1768 "	10,650	1821 "	87	
	1769 "	10,215	Total (20 years)		18,217
	1770 "	5,215	1822 (compulsory vaccination)		11
	1771 "	4,362	1823 "		39
	1772 "	5,435	1824 "		618
	1773 "	12,130	1825 "		1,243
	1774 "	2,055	1826 "		625
	1775 "	1,275	1827 "		600
	1776 "	1,503	1828 "		257
	1777 "	1,943	1829 "		53
	1778 "	6,607	1830 "		104
	1779 "	15,102	1831 "		612
	1780 "	3,374	1832 "		622
	1781 "	1,485	1833 "		1,145
	1782 "	2,482	1834 "		1,049
	1783 "	3,915	1835 "		445
	1784 "	12,456	1836 "		138
	1785 "	5,077	1837 "		361
	1786 "	671	1838 "		1,805
	1787 "	1,771	1839 "		1,934
	1788 "	5,462	1840 "		650
	1789 "	6,764	1841 "		237
	1790 "	5,893	1842 "		58
	1791 "	3,101	1843 "		9
	1792 "	1,939	1844 "		6
	1793 "	2,103	1845 "		6
	1794 "	3,964	1846 "		2
	1795 "	6,740	1847 "		13
	1796 "	4,503	1848 "		71
	1797 "	1,733	1849 "		341
	1798 "	1,357	1850 "		1,376
	1799 "	3,756	1851 "		2,488
	1800 "	12,032	1852 "		1,534
	1801 "	6,057	1853 "		279
Total (53 years)		1854 "		204	
		1855 "		41	
The population in 1751 was				1,785,727	
" " 1855 "				3,639,332	

SMALLPOX MORTALITY PER MILLION LIVING, SWEDEN, 1774 TO 1893.

Before vaccination.		Permissive vaccination.		Era of compulsory vaccination, 1817-1893.							
1774 . . .	1020	1802 . . .	644	1817 . . .	96	1845 . . .	2	1873 . . .	265		
1775 . . .	631	1803 . . .	611	1818 . . .	120	1846 . . .	1	1874 . . .	936		
1776 . . .	737	1804 . . .	605	1819 . . .	63	1847 . . .	4	1875 . . .	424		
1777 . . .	943	1805 . . .	449	1820 . . .	55	1848 . . .	21	1876 . . .	126		
1778 . . .	3178	1806 . . .	613	1821 . . .	14	1849 . . .	99	1877 . . .	79		
1779 . . .	7196	1807 . . .	884	1822 . . .	4	1850 . . .	395	1878 . . .	44		
1780 . . .	1593	1808 . . .	757	1823 . . .	15	1851 . . .	707	1879 . . .	31		
1781 . . .	699	1809 . . .	1007	1824 . . .	226	1852 . . .	433	1880 . . .	38		
1782 . . .	1165	1810 . . .	347	1825 . . .	449	1853 . . .	78	1881 . . .	65		
1783 . . .	1832	1811 . . .	291	1826 . . .	223	1854 . . .	57	1882 . . .	34		
1784 . . .	5810	1812 . . .	167	1827 . . .	212	1855 . . .	11	1883 . . .	27		
1785 . . .	2361	1813 . . .	225	1828 . . .	90	1856 . . .	14	1884 . . .	12		
1786 . . .	311	1814 . . .	126	1829 . . .	19	1857 . . .	132	1885 . . .	0.8		
1787 . . .	823	1815 . . .	191	1830 . . .	36	1858 . . .	345	1886 . . .	0.2		
1788 . . .	2534	1816 . . .	277	1831 . . .	211	1859 . . .	388	1887 . . .	0.6		
1789 . . .	3137			1832 . . .	213	1860 . . .	184	1888 . . .	1.5		
1790 . . .	2734			1833 . . .	387	1861 . . .	49	1889 . . .	0.4		
1791 . . .	1421			1834 . . .	352	1862 . . .	37	1890 . . .	0.2		
1792 . . .	878			1835 . . .	147	1863 . . .	76	1891 . . .	0.2		
1793 . . .	942			1836 . . .	45	1864 . . .	182	1892 . . .	0.8		
1794 . . .	1757			1837 . . .	117	1865 . . .	323	1893 . . .	5.0		
1795 . . .	2955			1838 . . .	583	1866 . . .	292				
1796 . . .	1963			1839 . . .	621	1867 . . .	252				
1797 . . .	751			1840 . . .	207	1868 . . .	342				
1798 . . .	585			1841 . . .	75	1869 . . .	354				
1799 . . .	1609			1842 . . .	18	1870 . . .	183				
1800 . . .	5126			1843 . . .	3	1871 . . .	78				
1801 . . .	2563			1844 . . .	2	1872 . . .	81				
Average, 2045		Average, 430		Average of 77 years, 155							

Change in the Age Incidence of Smallpox.—In the prevaccination days smallpox was *essentially a disease of children* and, indeed, was designated *Kindspocken* (childpox), or *Kindsblattern*. Owing to the extreme contagiousness and the almost universal susceptibility to smallpox the vast majority of people contracted the disease in childhood, and the adult population being made up largely of survivors was thus immunized. The conditions in relation to smallpox were much as they are at the present day in regard to measles. Comparatively few adults contract measles because the great bulk of the people pass through the disease in infancy.

As an instance of the incidence of smallpox among children in the prevaccination days, an epidemic occurring in 1795-96, described by Schwarz,¹ is here referred to. The epidemic occurred in Rawicz, Bojanowo, and Sarnowo in the Prussian province of Posen. The entire population of the three towns at the beginning of the epidemic was 13,329. Of this number 1252, or 9.4 per cent., were attacked with variola, and 199, or 1.5 per cent. of the population and 15.9 per cent. of the infected, died. At the end of the epidemic there were only 524 people remaining who were susceptible to the disease. The 1252 patients were of the following ages:

Under 5 years	743 persons, or 59.3 per cent.
Between 5 and 10 years	441 " 35.2 "
Over 10 years	68 " 5.2 "

¹ Quoted by Immerman, Nothnagel's Encyclopedia of Practical Medicine, p. 225.

It is thus seen that 94.8 per cent. of the patients were under ten years of age.

The almost exclusive mortality of smallpox among infants and children is also exemplified in the smallpox statistics of Kilmarnock from 1728 to 1764, a period of thirty-one years. During this time the total deaths were 3860, and the deaths from smallpox 622. There were nine epidemics of smallpox recurring at intervals of about four years. *Of the 622 smallpox deaths, 586 were in children under six years of age; 27 occurred in persons over the age of six, and the age of nine persons was not known.*

In *Chester*, in the epidemic of 1774, all of the smallpox deaths, numbering 202, occurred in children under ten years of age, and one-quarter of them under one year.

In Kilmarnock, of 622 deaths from smallpox between 1728 and 1763, only seven were of those above ten years.

In 1773, *Warrington*¹ sustained an epidemic of smallpox which resulted in 211 deaths (population 8000). In 1893 another epidemic occurred which resulted in 62 deaths (population 54,084, of whom 53,645 were vaccinated). The ages of the patients fatally attacked are tabulated as follows:

					SMALLPOX DEATHS.		
Age.					1893.		
					1773.	Vaccinated.	Not vaccinated.
Under	1 year	.	.	.	49	0	8 (under 1 month).
1	to 2 years	.	.	.	84	0	1
2	" 3 "	.	.	.	33	0	0
3	" 4 "	.	.	.	18	0	1
4	" 5 "	.	.	.	15	0	1
5	" 6 "	.	.	.	4	0	0
6	" 7 "	.	.	.	2	0	0
7	" 8 "	.	.	.	2	0	0
8	" 9 "	.	.	.	4	1	1
9	" 15 "	.	.	.	0	1	1
15	" 20 "	.	.	.	0	1	2
20	" 30 "	.	.	.	0	10	4
30	" 60 "	.	.	.	0	24	5
Over	60 "	.	.	.	0	1	0
					211	38	24

In 1773 *all of the deaths were under ten years, and nine-tenths were under five years of age.*

In 1893 among the vaccinated *not a death occurred under eight years of age; indeed, not one vaccinated child under eight years of age contracted smallpox.*

The statement may be considered as proven that vaccination has changed the age incidence of smallpox. *It is a rarity for a successfully vaccinated child under five years of age to die of smallpox.* It is even uncommon for a successfully vaccinated child under ten years to succumb to the disease, as will be seen from the following table compiled by the British Royal Vaccination Commission:

¹ Quoted by Edwardes, loc. cit.

SMALLPOX IN CHILDREN OF THE AGE OF 1 TO 10 YEARS.

Vaccinated.			Not vaccinated.		
Attacks	.	570	Attacks	.	1235
Deaths ¹	.	16	Deaths	.	375
Fatality	.	2.8 per ct.	Fatality	.	30.3 per ct.

The saving of infant life by vaccination should have reduced the general infant mortality in the postvaccination period; the following table shows that such a reduction in infant mortality did take place. It will be seen that the diminution in the general death rate of children under ten, and more particularly under five years of age, is far more pronounced than during adult life.

ANNUAL MORTALITY TO 1000 PERSONS LIVING. SWEDEN.

Ages.	Before vaccination.		After vaccination.	
	21 years (1755-1775).	20 years (1776-1795).	20 years (1821-1840).	10 years (1841-1850).
Under 5 years	90.1	85.0	64.3	56.9
5 to 10	14.2	13.6	7.6	7.8
10 " 15	6.6	6.2	4.7	4.4
15 " 20	7.6	7.0	4.9	4.8
20 " 30	9.2	8.9	7.8	6.8
30 " 40	12.2	11.6	11.8	9.8
40 " 50	17.4	16.1	16.7	14.5
50 " 60	26.4	23.9	26.0	23.6
60 " 70	48.1	49.3	49.4	46.3
70 " 80	102.3	104.1	112.9	102.8
80 " 90	207.8	197.4	243.7	228.5
90 " and upward	394.1	351.3	396.4	375.8
All ages	28.9	26.8	23.3	20.5

The *opponents of vaccination* urge that the decline of mortality from smallpox at the beginning of the nineteenth century was not due to vaccination, but to the *discontinuance of inoculation*.

It is probable that inoculation did tend to increase the *prevalence* of smallpox, but there is no evidence to prove that it increased the *mortality*. As the Royal Commission remarks: "It must be borne in mind that inoculated smallpox was on the whole much less fatal than that naturally acquired. The class of inoculated persons may thus have contributed less to the fatal cases of smallpox than if they had been left to the chances of natural contagion."

While inoculation was introduced into England in 1721, it found but little favor until 1740. The Suttons popularized the practice in 1763, and between 1770 and 1780 it was widely employed. Inoculation was therefore only practised on a large scale in England in the second half of the eighteenth century, and particularly in the last twenty-five years of this period. The antivaccinationists claim that the increase of smallpox mortality in the eighteenth century over the seventeenth was due to the practice of inoculation. If this were true, the mortality should have shown its increase particularly during the second half of the

¹ Six of these deaths occurred in children in whom the success of the vaccination was doubtful.

century. But the mortality was as great (if not greater) during the first quarter, when there was practically no inoculation, as during the last quarter of the century, when inoculation was greatly in vogue.

In *Sweden*, where inoculation was never practised to any extent, the fall in smallpox, after the introduction of vaccination, was as pronounced as in any country.

Again, it must be remembered that inoculation did not entirely cease in England upon the introduction of vaccination, but continued to be practised for a number of years, until it was declared illegal by act of Parliament in 1840.

It is evident from these considerations that the discontinuance of inoculation was to no appreciable extent the cause of the diminution of smallpox mortality at the beginning of the nineteenth century.

It has also been claimed by the opponents of vaccination that the decline in the prevalence of smallpox, dating from the beginning of the nineteenth century, was due to *improvement in sanitary conditions*.

It may be conceded that such improvements as better drainage and sewerage, freer ventilation, purer water supply, lessened crowding in dwellings, and the like would, by improving the average individual health, tend to lessen the fatality of all infectious diseases, not excluding smallpox. But such influences are totally inadequate to explain the striking and progressive decline in the prevalence and mortality from smallpox that followed the introduction of vaccination.

If sanitary improvements were responsible for the lessened mortality from smallpox, why did they not similarly influence the mortality from measles, scarlet fever, and whooping-cough, which are favored by the same conditions that aid the dissemination of smallpox? Smallpox and measles resemble each other in the sense that the spread of both diseases is not dependent upon any special sanitary defect. Unlike typhoid fever and cholera, their occurrence is influenced by personal infection rather than by any definite vices of sanitation. Measles and smallpox are the most contagious of all diseases; a momentary exposure of an unprotected person to the infection of smallpox or measles suffices for such individual to contract the disease. According to the Registrar General's Reports, during the same period in England that *smallpox* mortality has declined 72 *per cent.*, the mortality from *measles* has fallen only 9 *per cent.* Furthermore, the death rate from whooping-cough has declined but a little more than 1 *per cent.*, and the diminution in the mortality of scarlet fever has only become apparent within comparatively recent years. Again, the improvement in sanitation and mode of living has only caused a reduction of the general death rate of the country of 9 *per cent.*

Another noteworthy fact must not be forgotten—namely, that the decline in the death rate from smallpox has been entirely limited to persons below the age of fifteen. It is evident, therefore, that the lives of an enormous number of children have been saved. Above fifteen years of age the smallpox mortality for obvious reasons has not decreased. It is the height of absurdity to attempt to explain such an inequality

in the decline of smallpox mortality on the grounds of improved sanitation. The percentage of mortality borne by children the subjects of measles, scarlet fever, and whooping-cough does not differ materially from what it was a century ago.

Vaccination and Sanitation in Glasgow.—In 1780 the population of Glasgow was 43,832; by 1831 it had increased to 202,000. The area occupied was very small, and large and closely built tenement houses were erected to accommodate the growing population. Reports made in 1818, 1837, and 1838 indicated that the sanitary conditions were extremely bad, perhaps worse than those of any large town in Great Britain. Whooping-cough was on the increase and measles had become much more extensively prevalent. There was no disinfection and no isolation in hospitals. Despite all of these unfavorable conditions smallpox became decidedly less prevalent and less fatal. Before vaccination was practised, smallpox caused 19 out of every 100 deaths; within six years after the introduction of vaccination this number was reduced to 9 and after another period of six years to less than 4. Thus it is seen that with an increasing population, with *sanitation growing worse*, with measles deaths multiplying, the *mortality from smallpox decreased almost 80 per cent.*¹

Smallpox in the Vaccinated and Unvaccinated.—If vaccination had no protective influence against smallpox it would be logical to conclude that there should be no material difference between the mortality of this disease in vaccinated and unvaccinated persons. But the experience of over one hundred years offers *absolutely conclusive proof that there is a most pronounced difference in smallpox mortality in these two classes.* There has never been an epidemic of smallpox in any country of the world in which the death rate among the vaccinated has not been decidedly lower than that among the unvaccinated.

Epidemics of smallpox, like epidemics of all infectious diseases, vary greatly in malignancy. Diphtheria, scarlet fever, measles, and in fact all of the transmissible diseases appear at times in virulent form accompanied by high mortality, and at other times in mild form with correspondingly lower death rates.

These variations apply equally well to smallpox, and are produced by circumstances the nature of which are poorly or not at all understood. When severe epidemics of smallpox prevail the mortality rate is increased both among the vaccinated and unvaccinated. Variations in the severity of the disease, however, need not in the least degree complicate the comparative study of the fatality in the vaccinated and unvaccinated.

¹ Jenner Number of Public Health, May, 1896.

DEATH RATE OF SMALLPOX AMONG VACCINATED AND UNVACCINATED IN
VARIOUS COUNTRIES.

Places and times of observation.	Total number of cases observed.	Death rate per 100 cases.	
		Among the unvaccinated.	Among the vaccinated.
France, 1816-1841	16,397	16 $\frac{1}{8}$	1
Quebec, 1819-1820	?	27	1 $\frac{3}{8}$
Philadelphia, 1825	140	60	0
Canton Vaud, 1825-1829	5,838	24	2 $\frac{1}{8}$
Darkehmen, 1828-1829	134	18 $\frac{1}{5}$	0
Verona, 1828-1829	909	46 $\frac{2}{3}$	5 $\frac{2}{3}$
Milan, 1830-1851	10,240	38 $\frac{1}{3}$	7 $\frac{2}{3}$
Breslau, 1831-1833	220	53 $\frac{1}{5}$	2 $\frac{1}{10}$
Württemberg, 1831-1835	1,442	27 $\frac{1}{3}$	7 $\frac{1}{10}$
Carniola, 1834-1835	442	16 $\frac{1}{4}$	4 $\frac{2}{5}$
Vienna Hospital, 1834	360	51 $\frac{1}{4}$	12 $\frac{1}{3}$
Carinthia, 1834-1835	1,626	14 $\frac{1}{3}$	1 $\frac{2}{3}$
Adriatic, 1835	1,002	15 $\frac{1}{5}$	2 $\frac{1}{5}$
Lower Austria, 1835	2,287	25 $\frac{1}{5}$	11 $\frac{1}{9}$
Bohemia, 1835-1855	15,640	29 $\frac{1}{5}$	5 $\frac{1}{6}$
Gallicia, 1836	1,059	23 $\frac{1}{3}$	5 $\frac{1}{7}$
Dalmatia, 1836	723	19 $\frac{2}{3}$	8 $\frac{1}{4}$
London Smallpox Hospital, 1836-1856	9,000	85	7
Vienna Hospital, 1837-56	6,218	30	5
Kiel, 1852-1853	218	32	6
Württemberg, no date	6,258	38 $\frac{9}{10}$	3 $\frac{1}{2}$
Malta, no date	7,570	21.07	4.2
Epidemiological Society Returns, no date	4,624	19.7	2.9

The above figures show that among thousands of cases of smallpox occurring in cities all over the world, the *death rate from smallpox has been from five to sixteen times greater among the unvaccinated than among the vaccinated.*

VACCINATED AND NON-VACCINATED CASES OF SMALLPOX WHICH TERMINATED
FATALLY, ACCORDING TO OFFICIAL VACCINATION RETURNS (21 YEARS).
PRAGUE.

Year.	Cases of vacci- nation.	Remain- ing non- vacci- nated.	Smallpox.				Remarks.
			Cases.		Deaths.		
			Vacci- nated.	Non-vac- cinated.	Vacci- nated.	Non-vac- cinated.	
1835	132,727	4,029	505	430	20	136	One case of smallpox oc- curs among 367 $\frac{2}{3}$ vaccinated, 12 $\frac{1}{3}$ non-vaccinated.
1836	130,194	3,319	374	215	26	64	
1837	126,123	3,971	57	123	4	52	
1838	133,527	3,967	101	96	15	32	
1839	132,523	3,906	160	168	20	70	
1840	140,898	3,585	1138	966	89	351	One fatal case of smallpox occurs among 7166 $\frac{1}{3}$ vaccinated, 40 $\frac{2}{3}$ non-vaccinated.
1841	139,471	3,482	1583	1522	83	382	
1842	142,970	3,180	681	703	39	208	
1843	142,814	2,874	627	714	21	229	
1844	128,647	6,109	61	148	7	43	
1845	149,612	6,410	55	63	2	25	Among cases of smallpox died the 19th part of the vac- cinated, 3d part of the non-vac- cinated.
1846	146,467	5,475	6	50	...	7	
1847	141,268	5,361	19	25	...	4	
1848	132,320	5,718	227	169	17	49	
1849	139,523	5,704	575	645	63	177	
1850	156,561	6,314	568	374	14	131	
1851	152,294	4,694	16	293	3	43	
1852	161,364	3,689	252	231	12	65	
1853	145,088	3,067	327	168	3	39	
1854	161,318	2,927	457	203	7	61	
1855	136,424	2,349	389	156	8	56	
Total,	3,005,578	90,130	8178	7462	423	2224	
Average,	143.122 $\frac{14}{21}$	4.291 $\frac{19}{21}$	389 $\frac{9}{21}$	355 $\frac{7}{21}$	20 $\frac{3}{21}$	105 $\frac{19}{21}$	

In a period covering twenty-one years from 1835 to 1855 in Prague official returns show that whereas *one-third of all unvaccinated* cases of smallpox died, but *one-nineteenth of the vaccinated* cases succumbed to the disease.

The following figures of an epidemic of smallpox at Marseilles in 1828 indicate the marvellous fact that but $\frac{1}{2}$ per cent. of the vaccinated died of smallpox, whereas among the unvaccinated the death rate was 25 per cent. *The fatality among the unvaccinated was therefore fifty times greater than among the vaccinated.*

Marseilles, 1828.	Number.	Cases of smallpox.	Deaths by smallpox.
Total number of persons at the ages (0-30) which were almost exclusively susceptible	40,000	6,020	1,024
1. Protected by previous smallpox	2,000	20	4
2. Protected by vaccination	30,000	2,000	20
3. Unvaccinated	8,000	4,000	1,000

Chemnitz¹ (Saxony).—According to Dr. Flinzer the population of Chemnitz at the time of the epidemic of 1870-71 was 64,222; of this number 53,891, or 84 per cent., were vaccinated, and 5712, or 9 per cent., were unvaccinated; in addition 4652, or 7.3 per cent., had previously had smallpox.

Of the vaccinated 935 took the disease and 7, or 0.7 per cent., died; of the unvaccinated 2643 took the disease and 243, or 9.2 per cent., died. The mortality among the *unvaccinated was almost twelve times greater than among the vaccinated.*

The relative mortality from smallpox for the unvaccinated population was 326 times greater than for the vaccinated.

Waldheim² (Saxony).—The epidemic in this town from 1872-73 presents, according to Müller's figures, a similar condition of affairs. The population at the beginning of the epidemic was 5055, of whom 4713, or 93.2 per cent., were vaccinated, and 342, or 6.2 per cent., unvaccinated. Altogether 250 persons were attacked, of whom 66 died. Of 124 vaccinated persons 11 died, giving a mortality rate of 8.9 per cent. Of 126 unvaccinated who took the disease, 55 died, yielding a death rate of 43.7 per cent. *The relative mortality from smallpox for the unvaccinated population was sixty-nine times greater than for the vaccinated.*

The British Royal Commission on Vaccination presents the statistics of six recent epidemics in Dewsbury 1891-92, Warrington 1892-93, Leicester 1892-93, London 1892-93, Gloucester 1892-93 and Sheffield. A grand total of 11,065 attacks is collected; this number resulted in 1283 deaths, or 11.5 per cent., divided as follows:

	Vaccinated.	Unvaccinated.
Cases	8744	2321
Deaths	461	822
Per cent.	5.2	35.4

¹ Quoted by Immerman, loc. cit. ² Ibid.

The death rate is therefore *seven times greater among the unvaccinated than among the vaccinated.*

If children under ten years of age are alone considered, the result is still more remarkable.

		Children under the age of 10 years.	
		Vaccinated.	Unvaccinated.
Cases		589	1449
Deaths		16	523
	Per cent.	2.7	36

If vaccination confers no protection against smallpox, how can this signal difference in the death rates of the two classes be explained? Some influence must have been at work which caused the one class to suffer less fatality than the other.

Eliminating all children under one year of age (who might by reason of tender age fall easier prey to the disease) the Commission still found the most striking difference in the fatality. Among the vaccinated the death rate was 2.8 per cent. as compared with 30.3 per cent. in the unvaccinated.

It is impossible to evade the conclusion that vaccination, being the only circumstance to differentiate the two classes, must have been the influence operating.

The opponents of vaccination are fond of quoting the statistics of the epidemic at *Leicester* in 1892-93. The facts are as follows: Two vaccinated children were attacked with smallpox, neither of whom died. Of unvaccinated children of the same age period, 107 were attacked, of whom 15, or 14 per cent., died. Over ten years of age, 197 vaccinated persons were attacked, of whom 2 died, or 1 per cent. Of unvaccinated persons over ten years of age, 51 were attacked, of whom 4, or 7.8 per cent., succumbed. Surely there is nothing in these figures to disprove the efficacy of vaccination as a life-saving agent.

Evidence of Influence of Vaccination Against Attacks of Smallpox.—Thus far figures have been cited to prove that vaccination lessens the fatality of smallpox. It has been shown that the death rate of smallpox among the vaccinated is decidedly lower than among the unvaccinated, and that the relative mortality of smallpox among a vaccinated population is strikingly less than among an unvaccinated one. It remains to present evidence of the influence of vaccination in the attack rate of smallpox. The British Royal Commission on Vaccination gives the following census concerning the epidemic in Sheffield:

SHEFFIELD ATTACK RATE.			
Vaccinated population	268,397	Unvaccinated population	5715
Attacked by smallpox	4,151	Attacked by smallpox	552
Per cent.	1.55	Per cent.	9.7
Vaccinated children under 10 years	68,236	Unvaccinated children under 10 years	2259
Attacked by smallpox	353	Attacked by smallpox	228
Per cent.	0.5	Per cent.	10.1
Vaccinated persons 10 yrs. and upward	196,905	Unvaccinated persons 10 yrs. and upward	3429
Attacked by smallpox	3,774	Attacked by smallpox	322
Per cent.	1.9	Per cent.	9.4

It is seen from the above figures that the attack rate among vaccinated children under the age of ten years was only $\frac{1}{2}$ per cent., as compared with 10.1 per cent. among the unvaccinated. Over the age of ten the attack rate among the vaccinated was 1.9 per cent., and among the unvaccinated 9.4 per cent.

The following table, which presents the figures of five recent epidemics, gives results which are remarkably uniform:

	Attack rate under 10 years.		Attack rate over 10 years.	
	Vaccinated.	Unvaccinated.	Vaccinated.	Unvaccinated.
Sheffield . . .	7.9	67.6	28.8	58.6
Warrington . . .	4.4	54.5	29.9	57.6
Dewsbury . . .	10.2	50.8	27.7	58.4
Leicester . . .	2.5	85.8	22.2	47.6
Gloucester . . .	8.8	46.3	32.2	50.0

It is evident from the above comparisons that the lessened liability to attack among the vaccinated as compared with the unvaccinated is much more conspicuous among children under ten years of age than in a more advanced period of life.

Attack Rate in Invaded Houses.—In Sheffield, of 18,020 vaccinated persons of all ages living in infected houses, 4151, or 23 per cent., were attacked. Of 736 unvaccinated persons under the same conditions, 552, or 75 per cent., were attacked. When children under ten years are alone considered, the results are remarkable. Of 4493 vaccinated children in infected houses, 353, or 7.8 per cent., were attacked; of 263 unvaccinated children, 228, or 86.9 per cent., were attacked. *Ten out of eleven of the vaccinated children escaped, while but one out of eight of the unvaccinated children failed to take the disease.*

Similar ratios were noted in the epidemics in Leicester, Dewsbury, and Gloucester.

REVACCINATION STATISTICS.

It is a well-known fact that the protection conferred by vaccination against smallpox becomes impaired in the course of time and may, indeed, be lost entirely. The protection, however, may be restored by a second vaccination, and in the majority of individuals such revaccination will protect against smallpox for life.

It is, of course, understood that a person upon whom an unsuccessful revaccination has been performed is not revaccinated. Revaccination means a second attack of vaccinia and not merely the rubbing of virus into the skin. The failure of a secondary vaccination does not necessarily indicate an immunity against vaccinia and variola, but may be due to faulty virus or technique; or the subject may be for a time immune and later redevelop a susceptibility to both infections.

We have learned that vaccination lessens both the incidence and the mortality of smallpox. *Successfully revaccinated persons are attacked by smallpox much less frequently than those once vaccinated, and the mortality rate is further reduced.* In proof of this proposition the following statistical evidence gathered by the British Royal Commission on vaccination is presented.

During the epidemic of smallpox in *Sheffield* in 1887 there were in the town 64,431 revaccinated persons. Of this number 27 were attacked by smallpox, with 1 death. (This man had been revaccinated eighteen years previously, in 1869.) The *attack rate* of the revaccinated was, therefore, 0.04 per cent.

The attack rate of vaccinated persons over the age of ten, as enumerated in the census, was 1.9 per cent., and of the unvaccinated persons of the same age period 9.4 per cent.

In *Leicester*, during the epidemic of 1892-93, in a group of 133 houses with 842 inmates, 141 persons were attacked; among 84 revaccinated inmates but 1 was attacked. In another group of 60 houses there were 392 inmates, of whom 179 were attacked; among 31 revaccinated persons 5 contracted the disease.

In the first group the attack rate among the revaccinated was 1.1 per cent., as against 14.6 per cent. in the entire vaccinated class. In the second group of houses, which were evidently more intensely infected, the attack rate among the revaccinated was 16.1 per cent., among the vaccinated 35.3 per cent., and among the unvaccinated 59.6 per cent.

In *London* in 1892-93 there were 108 attacks in revaccinated persons, of which 101 were mild and 7 severe. In this class there were 4 deaths, showing a mortality of 3.7 per cent. Among vaccinated persons over ten the mortality was 4.2 per cent. and among the unvaccinated at this age period 20.9 per cent.

In *Warrington* in 1892-93 there were 64 revaccinated persons in the invaded houses; of these 8, or 12.5 per cent., were attacked. The percentage of vaccinated inmates attacked was 29.9 per cent. and unvaccinated 56.0 per cent. There were 41 inmates who had previously had smallpox; of this number 5, or 12.1 per cent., were attacked. There were no deaths among the revaccinated or among those suffering a second attack of smallpox.

The above evidence concerns comparatively recent epidemics. Revaccination was practised at an early date in some of the armies of the European countries, particularly among the *Württemberg* troops (1833). Heim says that in five years there occurred, among 14,384 revaccinated soldiers in *Württemberg*, only *one instance of varioloid*, and among 30,000 revaccinated persons in civil life only *two cases*, although during this time smallpox had prevailed in 344 localities and had produced 1674 cases of smallpox among the not revaccinated and in part not vaccinated population of 363,298.

In the *Baden* army between 1840 and 1868, according to Kussmaul, there were performed 100,546 revaccinations, of which 40,040, or 39.8 per cent., were successful. During this period of thirty-nine years there occurred in the army 359 cases of smallpox. Of this number only 34 were in the successfully revaccinated, while 325 were in the non-vaccinated, or, at least, in the unsuccessfully revaccinated.

Value of Revaccination as Illustrated in the Comparative Smallpox Losses of the French and German Armies in 1870.—The entire German field army, which numbered over a million soldiers, although

exposed to a raging smallpox epidemic in France, lost by death from this disease 297 *men*; the French army, on the other hand, suffered the enormous loss of 23,469 *men* from smallpox. (It will presently be shown that the German troops were well vaccinated and the French soldiers poorly vaccinated.)

The mortality rate from smallpox of the German soldiers in the field was 5.97 per cent. Of the stationary or immobile German troops 3472 were attacked, of whom 162 died, giving a mortality rate of 4.6 per cent. The aggregate number of German soldiers attacked, including those in the field and the stationary troops, was 8463, of whom 459, or 5.42 per cent., died.

The number of cases in the French army is not known, but the *death rate was forty-nine times greater than in the German army.*

Moreover, the death rate of smallpox in the German army compares very favorably with the death rate of the civil population of Germany. In the entire army, stationary and in the field, there were 459 deaths from smallpox; in the Prussian kingdom in 1871 there were 59,839 deaths from the same disease. Still more striking is the comparison of the death rate between the army and the inhabitants of Berlin. In this city of 826,341 population, a much smaller number than that comprising the army, the deaths from smallpox were 5508.

It is known that the *Prussian army*¹ *was well vaccinated* up to the time of the war, when the vaccine supply became insufficient. Nearly all of the soldiers of the German army had been vaccinated in childhood and again upon entrance into the army, for that custom had been enforced for a number of years.

The French army, on the other hand, was poorly vaccinated. From 1832 to 1859, smallpox caused 39 per cent. of all deaths in the French army. In 1857 an order was issued that all recruits be vaccinated without regard to the presence of previous scars, and the smallpox deaths during 1862-72 fell to 19 per cent., exclusive of the year of the war. It is evident, however, that vaccination was only partially practised, for official record shows that in 1866, of 45,064 recruits but 33,513 were vaccinated; in 1868, of 82,203 recruits only 47,324 were vaccinated, and in 1869, of 115,876 recruits only 54,720 were vaccinated; in other words, in 1869, 61,156, or over half the recruits, were not vaccinated on entrance into the army. Furthermore, a large proportion of the vaccinations performed were without result; of first vaccinations 51 to 63 per cent. failed, and on repetition 66 per cent. failed.

That locality did not cause the discrepancy in the death rate of the French and German soldiers is shown by the fact that the smallpox mortality among the French prisoners on German soil was 1963, while the entire German army on German soil lost but 162 men.

The remarkable results of vaccination and revaccination in the German army, particularly when compared with those in the French army and with the civil population of Germany, led to the adoption by the German

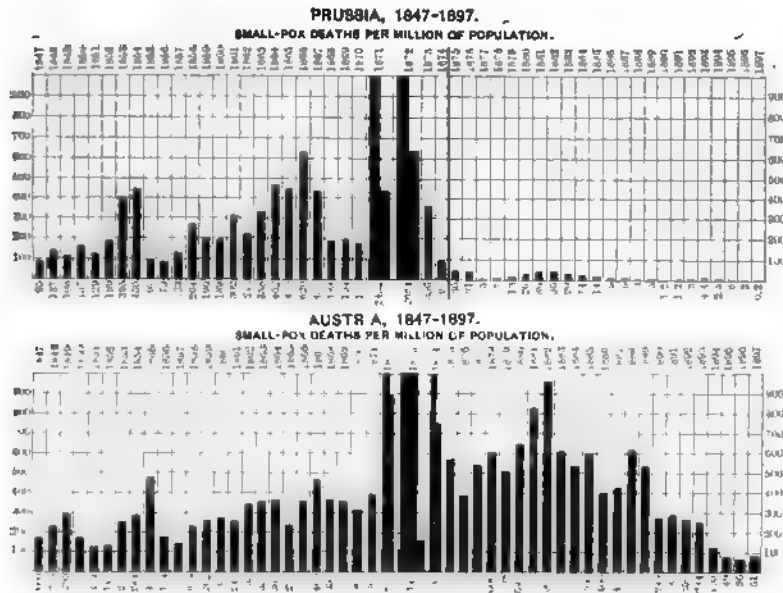
¹ Edwardes, loc. cit.

government of a law making vaccination and revaccination compulsory. This was passed April 8, 1874, and went into effect on April 1, 1875.

Its essential provisions are as follows: Every child must be vaccinated before the expiration of the first year of its life, unless it has had smallpox or unless some physical disability exists; in the latter event the vaccination is undertaken within one year of the removal of the existing disability. Every pupil of a public or private educational institution must be vaccinated between the age of thirteen and fourteen years, unless there is medical proof that he has had an attack of smallpox within five years or has been successfully vaccinated within that time.

Parents, caretakers, guardians, or heads of schools who fail to comply with the law are subject to fine or imprisonment. Vaccination must be performed only by physicians, and anyone vaccinating illegally is punished by a fine not exceeding 150 marks or imprisonment not exceeding fourteen days.

FIG. 18



Tables showing the decline of smallpox in Germany after the enactment of compulsory vaccination in 1874; smallpox mortality is compared with that of Austria

The Results of the German Compulsory Vaccination Law.—If there was in existence no other statistical evidence of the efficacy of vaccination and revaccination, the history of smallpox in Germany since 1875 would be all sufficient testimony.

From 1816 to 1870 the annual mortality from smallpox in Prussia varied from 7.32 to 62.0 per 100,000 of population. This death rate was small compared with the prevaccination periods.

During the disastrous pandemic of 1871-72 the rate was 243.2 and 262.67, respectively. After the law of 1875 went into effect the annual

mortality in Prussia fell so that between 1875 and 1886 the average yearly mortality per 100,000 of population was 1.91, the maximum reaching 3.6 (in 1877).

On the other hand, in Austria, where the lax vaccination and revaccination requirements remained unchanged, the mortality rate from smallpox during about the same period (1875 to 1884) increased, varying between 39.28 (1876) and 94.79 in 1882. (See Fig. 18.)

The results of the German vaccination law in the principal states of the Empire are given in the following table:

THE RESULTS OF THE GERMAN VACCINATION LAW, 1874.					
(Smallpox deaths per million living.)					
1. Before the law of 1874.					
Year.	Prussia.	Bavaria.	Württemberg.	German Empire.	Contrast Austria.
1866	620	120	133	... ¹	368
1867	432	250	63	...	484
1868	188	190	19	...	370
1869	194	101	74	...	374
1870	175	75	293	...	293
1871	2482	1045	1130	...	383
1872	2624	611	637	...	1866
1873	356	176	30	...	3094
1874	95	47	3	...	1725
2. Since 1874.					
1875	36	17	3	...	576
1876	31	13	1	...	406
1877	3.4	17	2	...	555
1878	7.1	13	0	...	631
1879	12.6	5	0	...	534
1880	26	12	5.6	...	674
1881	36.2	15	3.6	...	807
1882	36.4	12	6.6	...	947
1883	19.6	6	35.2	...	596
1884	14.4	1	11.6	...	530
1885	14	3	0	...	600
1886	4.9	1	1	4.2	400
1887	5	1.8	0	3.5	417
1888	2.9	3.8	0.5	2.3	615
1889	5.4	5.2	0	4.1	537
1890	1.2	1.5	0	1.2	249
1891	1.2	1.2	0	1.0	287
1892	3	0.5	0	2.1	256
1893	4.4	0.7	1	3.1	244
1894	2.5	0.3	0	1.7	105
1895	0.8	0.2	0	0.5	49
1896	0.2	0.2	0	0.2	36
1897	0.2	0	0	0.1	61
1898	0.4	0.3	0	0.3	
1899	0.5	

The remarkable results of compulsory vaccination and revaccination in Germany are perhaps the more striking when the mortality rate of smallpox in German cities is compared with cities of other countries. After compulsory revaccination in 1875 the average annual death rate from variola from 1875 to 1886 in the following cities was as follows:

¹ No statistics.

DEATH RATE FROM SMALLPOX PER 100,000 OF POPULATION.

German Cities.		Other Cities.	
Berlin	1.16 persons.	Paris	26.24 persons.
Hamburg	0.74 "	St. Petersburg	35.82 "
Breslau	1.11 "	Vienna	64.90 "
Dresden	1.03 "	Prague	147.90 "

There is but one explanation for the marvelously low death rate in the German cities as compared with other continental centres; that explanation is *careful and universal vaccination and revaccination*.

A comparison of total *smallpox attacks* in the German, French, and Austrian armies after 1875 is equally instructive:

German army (1875-1887)	148 men.
French army (1875-1881)	5,605 "
Austrian army (1875-1886)	10,238 "

In the German army, despite greater numbers and a longer period of time, the smallpox attacks were enormously less than in the French and Austrian armies.

Since the law of 1875 went into effect in Germany, *there have been no epidemics of smallpox in that country*. The smallpox is frequently introduced by foreigners, particularly on the frontiers, but the disease can find no foothold. In 1899 there occurred in the German Empire, among 54,000,000 people, 28 deaths from smallpox; these occurred in twenty-one different districts, the largest number in any one district being 3. Not a case occurred in a large town.

Kübler¹ in speaking of the importation of smallpox into Germany, says: "Among the fatal cases there were many who had come from foreign countries; in the interior of the Empire aliens, chiefly Russian-Polish laborers, constituted a large percentage of those who contracted the disease. The annual recurrence of the pestilence among these people has recently necessitated a regulation that workmen before being admitted to employment within the realms must produce proof of successful vaccination or recovery from an attack of smallpox, and in case they were unable to do so they must submit to vaccination."

The following figures indicate the prevalence of smallpox on the German frontier as compared with the interior.

The mortality from smallpox in Germany from 1886 to 1889 was:

	At the Frontier.	In the Interior.
1886	110 cases.	45 cases.
1887	119 "	49 "
1888	94 "	16 "
1889	188 "	12 "

In 1897 there were but five deaths from smallpox in the entire German Empire (54,000,000 population).

Furthermore, for a *period of thirteen years* in a population comprising two-fifths of the total inhabitants of Germany, there were *only five instances of death from smallpox in successfully revaccinated persons*.

¹ Geschichte der Impfung und Blattern, 1901.

Germany has taught the world how to utilize Jenner’s great discovery so as to exterminate smallpox.

The German Vaccination Commission of 1884, referring to the influence of the compulsory vaccination law, says:

“Previously to 1871 smallpox mortality in Austria behaved much like that of Prussia, though higher on the whole. The great epidemic of 1872–74 was more fatal and lasted longer than in Prussia. During the next two years the mortality fell, as usual after epidemics. Here the influence of the epidemic in lowering the mortality ceases, and the latter rises at once to its old figures, viz., as before the epidemic, and even higher, and this rise was not merely temporary.

“The remarkable and persistent decline in Prussia since 1875 can only be due to the vaccination law of 1874, *because all other conditions remain the same in the two countries.* The only difference is that in Prussia the revaccination of all school-children at the age of twelve years was made compulsory in 1874.”

The Board of Health of Berlin has prepared tables comparing the number of deaths occurring between the years 1886 and 1889 in countries having compulsory vaccination, and those without such provision:

Population.			Smallpox deaths.				Average of deaths.	Average per million of population.
			1886.	1887.	1888.	1889.		
Compul'y vacci'n.	Sweden,	4,746,465 . .	1	5	9	2	4	1
	Ireland,	4,808,728 . .	2	14	3	0	5	1
	Scotland,	4,013,029 . .	24	17	0	6	12	3
	Germany,	47,923,735 . .	197	168	112	200	169	3.5
	England,	28,247,151 . .	275	505	1,026	23	458	16
	Switzerland,	2,922,430 . .	182	14	17	3	54	18.5
	Belgium,	5,940,365 . .	1,213	610	865	1,212	975	164
	Russia,	92,822,470 . .	16,938	25,884	1.....	1.....	21,411	231
	Austria,	23,000,000 . .	8,794	9,591	14,138	12,358	11,220	510
	Italy,	29,717,982 . .	1.....	16,249	18,110	13,416	15,925	536
	Spain,	11,864,000 . .	1.....	1.....	14,378	8,472	11,425	963

But a glance is necessary to show the striking difference between the number of deaths in those countries having compulsory vaccination and those in which there is no such measure. The average deaths per million in the compulsory vaccination countries is *eighty times less* than in the others. Furthermore, England is the least vaccinated of the compulsory countries and her death rate is the highest among these.

The Imperial Board of Health of the German Empire gives the frequency of smallpox in various European countries between 1893 and 1897 inclusive, a period of five years.²

¹ No statistics. ² Quoted by Kübler, loc. cit.

PLATE IV.



Two Sisters Suffering from Smallpox.

The one on the right, aged fourteen, was successfully vaccinated in infancy: she contracted a mild varioloid and recovered without any scarring. The other, unvaccinated, developed a severe smallpox, confluent on face and arms, finally recovering although considerably pitted.

PLATE V.



Same Patients as in Plate IV., showing Appearance after Recovery.

THE FREQUENCY OF SMALLPOX IN EUROPEAN STATES BETWEEN 1893-1897
INCLUSIVE (5 YEARS).

Country.	Population	Average yearly mortality in every million population.	Actual number smallpox deaths.	Years.
Germany	52,042,282	1.1	287	5
Denmark	793,356	0.5	2	5
Sweden	4,894,790	2.1	41	4
Norway	2,045,900	0.6	5	4
England and Wales	30,889,524	20.2	3,066	5
Scotland	4,155,886	12.3	256	5
Ireland	4,580,655	9.9	226	5
Switzerland	3,032,901	5.1	79	3
Netherlands	4,797,249	29.7	929	5
Belgium	5,419,498	99.9	3,208	5
French States	8,283,079	90.2	3,721	5
Russian Empire including Asiatic Russia	118,950,400	468.2	275,502	5
Austria	28,000,000	99.1	11,769	5
Italy	31,007,422	72.7	11,278	5
Spain	10,596,649	563.4	23,881	4
Hungary	18,284,916	184.3	12,241	5

Here, again, the countries which during this period have the most stringent vaccination laws suffer the least smallpox, namely, Germany, Denmark, Sweden and Norway.

In well-vaccinated Germany, but one person a year in every million died of smallpox.

In England and Wales, where vaccination is generally but not universally practised, 20 persons per million died each year.

In Austria, where the vaccination laws are poorly enforced, 99 persons per million died each year.

It is, indeed, quite possible to know to what extent vaccination is practised in the various countries by noting the mortality from smallpox.

There is an inverse proportion between these factors. It is evident, therefore, that in Spain and in Russia (including Asiatic Russia) vaccination must be greatly neglected.

The tables teach another lesson, namely, that without vaccination smallpox is still to be regarded as a dread scourge, as a great destroyer of human life. For in the five years from 1893 to 1897, in the sixteen countries mentioned, 346,520 lives were sacrificed to smallpox; of this number Russia lost 275,502. These figures are the more terrible when it is recognized that these lives might have been saved by the application of a prophylactic measure within the reach of all.

Immunity of Physicians and Nurses in Smallpox Hospitals.—If it can be demonstrated that physicians and nurses in smallpox hospitals are protected by vaccination, this must be regarded as a crucial test. For if these persons, living in the same atmosphere with scores or hundreds of smallpox patients, breathing in their very exhalations, are enabled to escape the infection, it certainly should be possible for others much less exposed to acquire similar immunity.

Experience shows that physicians, nurses and others, if recently successfully vaccinated, may live in smallpox hospitals with perfect safety. The

immunity of employés (when properly revaccinated) is a uniform experience in practically all smallpox hospitals.

In the hospitals of London, from 1876-79, there were admitted 11,412 smallpox patients who had been vaccinated in infancy, but not a single case was known to have occurred in a person who had been successfully revaccinated. It was the rule to revaccinate all nurses and employés before entering the hospital, and the number thus employed amounted to about 1000; of these only some half-dozen took smallpox, and they, for some cause or other, had escaped revaccination.

Dr. Marson,¹ physician to the Smallpox Hospital of London for many years, giving evidence in 1871, stated that *during the preceding thirty-five years no nurse or servant at the hospital had been attacked with smallpox*. Since that period one case only has occurred, and that in an unrevaccinated gardener. Thus, during a period of sixty years but one case of smallpox has occurred among hundreds of persons who were in the closest contact with the disease. Dr. Marson took the precaution of revaccinating all persons before permitting them to go on duty. Dr. Collie,² whose experience is also large, says: "During the epidemic of 1871, out of 110 smallpox attendants at Homerton, all but 2 were revaccinated, and these 2 took smallpox."

At a meeting of the German Vaccination Commission (1884) Dr. Eulenburg related "that a manufacturer in Posen had all his workmen vaccinated except one, who refused. This man alone of the 150 took smallpox shortly afterward and died."

In 1885 a committee of the Epidemiological Society of London reported that out of 1500 attendants in smallpox hospitals, 43 took smallpox and *not 1 of the 43 had been revaccinated*.³

"The experience of the epidemic of 1876-77 was of the same kind, all *revaccinated attendants having escaped*, while the only one who had not been vaccinated took the disease and died of it."⁴

In the epidemic of 1881 in London, of 90 nurses and other attendants of the Atlas Smallpox Hospital Ship, the only person who contracted smallpox was a housemaid who had not been revaccinated.⁵

Dr. T. F. Ricketts,⁶ the medical superintendent of the Smallpox Hospital Ships on the Thames, shows that *out of 1201 persons in attendance on board the smallpox ships since 1884, only 6 contracted the disease*, and all recovered. None of these persons had been successfully revaccinated before going on duty.

At the Southampton Fever Hospital all persons employed during the smallpox epidemic of 1893 were revaccinated before going on duty, and, although freely exposed to the disease, not a single individual contracted smallpox.⁷

According to Dr. Hill, of Birmingham, during the epidemic in 1893 over 100 persons were employed at the City Smallpox Hospital, all of

¹ E. J. Edwardes, *The Practitioner*, May, 1896.

² *Ibid.*, loc. cit.

³ *Transactions of the Epidemiological Society*, vol. v., new series.

⁴ Dr. Collie, *Quain's Dictionary of Medicine*.

⁵ Mentioned by Ernest Hart. *Allbutt's System of Medicine*.

⁶ *Report of the Metropolitan Asylums Board for 1892*.

⁷ Hart, loc. cit.

PLATE VI.



Three Members of a Family Brought to the Municipal Hospital with the Mother who was Suffering from Smallpox

The child in the cradle was unvaccinated; the other two, the 1 year old child, a good before the onset of the smallpox epidemic. These two children remained in the hospital wards several weeks and the mother was discharged.

whom had been recently revaccinated; *not one of them contracted smallpox.*

In the Municipal Hospital of Philadelphia during a period of thirty-four years, in which time over 9000 cases of smallpox have been treated, *we have not had a physician, nurse, or attendant who had been successfully vaccinated or revaccinated prior to going on duty, contract the disease.*

Indeed, during all of these years and among hundreds of persons in attendance on the sick, only two or three fell ill with mild attacks of varioloid, and these would have been avoided had not the exigencies of the occasion demanded that the attendants be immediately assigned to duty, without waiting for the vaccination to work out its immunity.

Physicians, nurses, and others have no such immunity against other infectious diseases as against smallpox. According to Ernest Hart,¹ in 1893, of 2484 persons employed in the nine Metropolitan Fever Hospitals of London, 130 became infected and 2 died; 4 assistant medical officers, 10 nurses, 43 assistant nurses, and 16 maid-servants were attacked with scarlet fever. Two assistant medical officers, 6 nurses, and 15 assistant nurses contracted diphtheria.

The deaths from smallpox of *medical men* (who are particularly well vaccinated) are but 13 *per million* as against 73 *per million of the general population* in England. In scarlet fever, on the other hand, against which physicians have no special protection, the figures are reversed; 59 *medical men per million die of scarlet fever* as against 16 *per million of the general population.*

Experience of the Municipal Hospital of Philadelphia during the Epidemic of 1901-1904.—During this period over 3500 cases of smallpox were received at the hospital. No person who had been recently successfully vaccinated was admitted to the hospital with smallpox. Since the outbreak of the disease in the city, it has been estimated that about 500,000 persons were vaccinated—about a third of the population. If vaccination confers no protection against smallpox, it is reasonable to suppose that some of these persons would have contracted the disease and been brought to the hospital. (About 80 per cent. of all the cases in the city were sent to the hospital.) But no such patient could be found among over 3500 admissions.

In order to provide accommodations for the unusually large number of cases of smallpox, which was rapidly increasing, it was necessary to erect additional buildings as well as enlarge those already in use. On this work from 50 to 60 men were employed, and as they were required to come constantly into close proximity to the patients they were all requested to come to the administration building and get vaccinated. This request was complied with by all except 2, and these 2 took smallpox. We would emphasize the fact that they were the only ones that were stricken by the disease. One we understand was a Christian Scientist, and he trusted to this delusion for his protection. Poor fellow! It did not even save his life, as he fell a ready victim to a disease that respects nothing but vaccination.

¹ Loc. cit.

Later, it was found necessary to enlarge still further some of these buildings, and other workmen were engaged. Two of these, for some reason which we never learned, neglected to get vaccinated before commencing the work, and they both took smallpox.

FIG. 19



Two children in the Municipal Hospital are unvaccinated and the other vaccinated on the day of admission. The scars are still seen upon the leg. This child remained in the hospital with his mother who was suffering from smallpox for three weeks and was discharged perfectly well. The unvaccinated child admitted with smallpox died.

For the last five years the medical schools of Philadelphia have had the privilege of sending their more advanced students to the Municipal Hospital for clinical instruction in the various contagious and infectious diseases therein treated. During this period over 700 students have visited the smallpox pavilions and have studied the patients. One of the requirements was that each student had to show evidence of protection, either by having been recently successfully vaccinated or by

not responding to vaccination after two or three careful trials. Of the entire number of students *one* contracted smallpox, and it was subsequently found that he had never been successfully vaccinated.

Since the present epidemic began, about 200 persons, including physicians, nurses, ward maids, cooks, laundresses, and the like, have been employed in the smallpox department, and *not one* has contracted the disease.

These facts are not wondered at by those who are familiar with smallpox; they are anticipated. Evidence of this same nature has accumulated for nearly a half-century. Every epidemic adds fresh data. The immunity of revaccinated nurses and physicians against smallpox constitutes testimony in favor of the efficacy of vaccination which is irrefutable.

Further Direct Evidence of the Efficacy of Vaccination.—Much convincing evidence of the protection afforded by vaccination against smallpox never appears in morbidity or mortality statistics. Every physician who is familiar with smallpox can cite numerous instances of such protection. Jenner and other early vaccinators established direct proof of the virtue of vaccination by showing that smallpox could not be given to an individual recently successfully vaccinated.

Dr. Jenner in 1801 wrote: "Upward of 6000 persons have now been inoculated with the virus of cowpox, and the far greater part of them have since been inoculated with that of smallpox, and exposed to its infection in every rational way that could be devised, without effect." And Dr. Woodville, in 1802, stated that within two years there were vaccinated at the Smallpox Hospital 7500 persons, of whom about one-half were subsequently inoculated with smallpox matter, and in none of them did smallpox produce any effect.

Smallpox is one of the most highly contagious of all diseases, and nearly every human being is susceptible to it; we could cite scores of instances of protection granted to persons by vaccination after admission to the Municipal Hospital. A few examples which occurred during the recent epidemic (1901-04) and of which we have notes will suffice.

A child of one year, who had been successfully vaccinated about ten days before admission, was sent to the hospital with roseola vaccinosa which had been diagnosed as variola. The child remained in the smallpox wards about three weeks and continued perfectly well. Another child, of nine years, with exactly the same history, returned home perfectly well after a constant exposure of over three weeks. An unvaccinated colored child, about two years old, was brought into the hospital with a sister who was suffering from smallpox. Immediately after admission vaccination was performed, and although the child was constantly exposed to the infection for three weeks he did not take the disease. Several other children and also some adults, who were sent to the hospital under erroneous diagnosis, were vaccinated for the first time after admission and were rendered absolutely immune.

In every epidemic of smallpox that has occurred in Philadelphia within the past thirty years, instances have been observed of whole

families being removed to the hospital because of an outbreak of the disease in these families. In such instances the unvaccinated children have suffered and often perished, while those who were vaccinated remained perfectly exempt, although living, eating, and sleeping in the infected atmosphere for several weeks. *But we have yet to see unvaccinated children escape the disease under similar conditions of exposure.* Furthermore, we have more than once seen a vaccinated infant take its daily supply of nourishment from the breast of its mother who was suffering from varioloid, and the infant continue as free from smallpox as if the disease were one hundred miles away and the food derived from the most wholesome source. This is evidence of the prophylactic power of vaccination that does not appear in mortality reports nor in statistical records.

Ravages of Smallpox in Countries where Vaccination is Neglected.—In most of the European countries and in the United States smallpox at the present day is a comparatively rare disease, appearing, as it does, in epidemics at infrequent intervals. Many physicians who have been in practice for fifteen or more years have never encountered even a single case of this disease. In well-vaccinated countries the epidemics are small and of short duration. In countries, however, in which vaccination is neglected, the epidemics may attain in extent and mortality the terrible numbers that were reached in the days before vaccination. In the Russian Empire, including Asiatic Russia, there were 275,502 deaths from smallpox in the five years from 1893 to 1898. In Spain, with a population of only ten and a half million people, there were 23,881 deaths from smallpox during this period. Hungary had 12,241 deaths, and Italy and Austria each over 11,000 deaths. In Germany, where there is compulsory vaccination and revaccination the smallpox deaths during the same five years numbered only 287.

Dr. Jeanselme¹ is authority for the statement that smallpox is still a murderous disease in Indo-China and other parts of the East. He estimates that a quarter of the infantile population succumbs to this disease. During times of epidemic recrudescence the death rate is higher still. In 1900 Dr. Jeanselme saw the population of the village of Loos almost completely swept away by smallpox, a few old people, protected by a previous attack, being the only survivors.

Children under the age of five years furnish the greatest number of victims. The Annamites and Cambodgians regard variola as a necessary evil, and children who have not gone through it practically do not count as members of the family. Vaccination is greatly neglected, but inoculation is practised. The blind in Indo-China are numerous, the loss of vision in large part being due to smallpox.²

The above conditions might readily prevail in all countries if the opponents of vaccination were successful with their propaganda.

¹ Quoted in the British Medical Journal, August 16, 1902.

² Ibid.

UNANIMITY OF OPINION AS TO THE VALUE OF VACCINATION.

There has probably never been in the history of mankind a great discovery the acceptance of which some men did not dispute. The great truth which Jenner gave to the world offers no exception to this general statement. There are dissenters who do not believe in vaccination, but they are chiefly to be found outside of the medical profession. *We know of no eminent physician who is not convinced of the efficacy of vaccination*; those physicians who have had a large practical experience with smallpox are the most ardent advocates of vaccination, for they have had the best opportunity of noting the behavior of vaccinated individuals in the presence of smallpox. The few physicians who are found in the ranks of the antivaccinationists are usually men without practical experience in smallpox; they argue with statistics (often wittingly or unwittingly distorted) and not with facts derived from personal observation.

As a prophylactic remedy against smallpox vaccination was generally accepted by the medical profession at an early date.

In 1856 the Medical Officer of the London Board of Health, John Simon, sent circular letters to 542 prominent members of the medical profession in the United Kingdom and in some of the other European countries, requesting their opinions as to the value of vaccination. Five hundred and thirty-nine replies were received and there was *absolute unanimity* as to the efficacy of vaccination as a protective measure against smallpox.

The most distinguished medical bodies in every country have time and time again affirmed their confidence in the protective influence of vaccination, and the most enlightened nations of the earth have officially recognized its value and have encouraged its practice.

Thomas Jefferson's appreciation of the value of Jenner's discovery may be judged from the following letter addressed to the discoverer of vaccination:

MONTICELLO, VIRGINIA, May 14, 1806.

SIR: I have received a copy of the evidence at large, respecting the discovery of the vaccine inoculation, which you have been pleased to send me, and for which I return you many thanks. Having been among the early converts of this part of the globe to its efficacy I took an early part in recommending it to my countrymen. I avail myself of this occasion to render you my portion of the tribute and gratitude due to you from the whole human family. Medicine has never before produced any single improvement of such utility. Harvey's discovery of the circulation of the blood was a beautiful addition to our knowledge of the ancient economy; but on a review of the practice of medicine before and since that epoch, I do not see any great amelioration which has been derived from that discovery. You have erased from the calendar of human afflictions one of its greatest. Yours is the comfortable reflection that mankind can never forget that you have lived; *future nations will know by history only that the loathsome smallpox has existed*, and by you has been extirpated. Accept the most fervent wishes for your health and happiness, and assurance of the greatest respect and consideration.

TH. JEFFERSON.

Thomas Jefferson's prophecy that "future nations will know by history only that the loathsome smallpox has existed" fails of fulfilment only because vaccination and revaccination are not universally adopted.

OPPOSITION TO VACCINATION.

It is a remarkable fact that, despite one hundred years of incontrovertible testimony of the value of vaccination, there should still exist at the present day an organized antivaccination movement. To be sure the active opponents of vaccination comprise but a very small percentage of the people, but their influence is none the less noxious. Curiously enough the opposition to vaccination is most acute in the very country whence this great discovery sprang; this fact is a sad commentary upon the common sense of this portion of the English population. The opponents of vaccination include a number of persons of prominence in the literary world; indeed, a large library of antivaccination literature has gradually arisen.

No great truth is ever promulgated that does not meet with opposition; the *truth of the value of vaccination has satisfied the judgment of medical men*, but a certain number of individuals outside of the profession dissent therefrom. These persons have, in various countries, banded together to antagonize the practice of vaccination and to oppose its compulsory enforcement.

We prefer to look upon these persons as *misguided* rather than regard them in a less charitable light. The evidence in favor of vaccination is so strong and irrefutable that an unbiased student of the subject can arrive at but one conclusion. There is no truth more clearly established than that vaccination and revaccination properly performed protect against smallpox. And yet some antivaccinationists persist in misinterpreting facts and figures with a view of discrediting vaccination; this is often so patent as to clearly establish the effort as wilful perversion. *Antivaccination propaganda have caused many innocent victims to be consigned by smallpox to a premature grave.*

There is but one rational argument for opposition to vaccination, namely, that the practice of this measure is not entirely devoid of some danger. But the danger is so slight in any individual instance that it is almost a negligible quantity. No human act is completely unattended with risk. When the rare instances of death following vaccination are compared with the frightful slaughter of thousands by smallpox before the days of vaccination, and even at the present day in countries where vaccination is neglected, the benefits of Jenner's God-given discovery may be appreciated.

CHAPTER III.

THE VARIOLOUS DISEASES OF LOWER ANIMALS.

A NUMBER of domesticated animals appear to be susceptible to pock diseases which are more or less closely allied to human smallpox. These affections are, by reason of difference in behavior, divisible into two natural groups. The diseases comprised in the first group are communicable through the atmosphere; they are accompanied by a generalized eruption, and may be regarded as death-dealing pestilences; in this class are to be included human variola and sheeppox. In the second group the diseases are only capable of transmission by inoculation (accidental or intentional); the eruption is usually limited to the sites of inoculation, and death rarely takes place. In the second group belong cowpox, horsepox, apepox, and other domestic animal pock diseases presently to be described.

Jenner was firmly of the belief that many of the common farm animals were subject to eruptive diseases allied to variola. He says:¹ "Our domestic animals are subject to a variety of eruptive diseases—the horse, the cow, the sheep, the hog, the dog, and many others. Even poultry come in for their share. Again, there certainly must be a reason why the term *chicken* is annexed to a species of pock which infests the human skin. In the province of Bengal the poultry are subject to eruptions like the smallpox, which becomes epidemic and kills them by the hundreds."

Dr. Baron² says: "It seems certain that there are, at least, four animals—namely, the horse, the cow, the sheep and the goat—which are affected with a disorder communicable to man, and capable of securing him from what appears to be a malignant form of the same disease. It is, moreover, proved that other animals may take the vaccine disease by inoculation, and that matter taken from pustules so produced affords the genuine cowpox in man. The animals on which these experiments have been tried are the dog, the goat, the she-ass, and the sheep. The fact as regards the dog was ascertained by Dr. Jenner."

Indeed, Jenner alleges to have found *dogs* very susceptible of the variolæ vaccinae; he believed that an attack of this disease rendered the dog immune against the distemper.

Smallpox of Sheep.—*Sheeppox*, *variola ovina*, or *clavelée*, is an acute contagious and epizootic disease characterized by symptoms closely simulating the manifestations of variola in the human subject.

Variola ovina is supposed to have arisen in Asia, and, like smallpox, to have extended thence to the continent of Europe. Various countries

¹ Manuscript of Jenner, quoted by Baron.

² Life of Jenner, p. 243.

have, from time to time, experienced devastating epidemics which have greatly interfered with the sheep-growing industry.

The period of incubation of the disease is somewhat variable, but is ordinarily between nine and twelve days. It is stated that sheep may now and then remain unaffected for a period of one or even two months, although intimately exposed to the contagion of the disease. Some Continental observers state that the eruption is preceded by two or three days of fever, but Simonds and other English writers affirm that in their experience they have never noted any illness prior to the appearance of the eruption.

At this time the infected sheep separates himself from his fellows, looks weak and dejected, lies down and refuses food, although he will drink water freely. The breathing is quick and short and the heart beats accelerated. The conjunctivæ are reddened, the lids swollen, and the tears trickle down the face. A mucous discharge issues from the nose and tends to block the nostrils. These symptoms begin synchronously with the eruption and continue until vesiculation begins, when there is commonly an abatement of these manifestations.

The eruption appears as florid-red papules, which are firm and unyielding to the touch. These are usually observed first on the inner side of the extremities, and on the cheeks and lips, where the skin is hairy, but not covered with wool. Nude portions of the body, such as the prepuce, labia, anus, and inferior surface of the tail may be simultaneously attacked. The eruption rapidly spreads over the entire integument, manifesting itself either in a discrete or confluent form. In certain species the face is profusely involved, in which case the disease proves extremely fatal.

The duration of the papular stage may vary between two and six days, averaging three in the majority of cases; this stage is somewhat protracted in confluent cases. The reddish papules become gradually converted into whitish vesicles containing a limpid fluid. Many of the vesicles are small, and nearly all are unilocular, contrasting in this respect with the multilocular character of the vesicles in human variola. The transformation of the papules into vesicles is not uniform, some undergoing this change a day or two after others, while some papules may disappear without vesiculating at all. The vesicles are not surrounded by an areola at an early stage, but only after they have fully matured. In the perfectly formed vesicle of sheeppox a central depression may be seen, but this is far from being constant.

The duration of the vesicular stage is variable. In the milder cases the eruption may not progress beyond the stage of vesiculation, and pustules may therefore be absent. In severe and protracted cases, however, a purulent fluid is secreted and the vesicles are converted into pustules. Deep ulcerations may develop when a large quantity of pus is produced; in confluent cases the inflammation may be so severe as to lead to patches of gangrene, particularly upon the abdomen and legs.

The stage of vesiculation or pustulation is followed by crusting of

the lesions, constituting the process of desiccation. The scabs are of a brownish-yellow or blackish color, and vary considerably in volume. When these fall off *pits* are seen in the skin, which vary in depth according to the severity of the disease. Two to four weeks may elapse before the complete healing of the sores. At the sites of the lesions permanent defects remain in the wool of the animal.

In confluent cases the fever remains high, there is rapid respiration, moaning, frothy discharge from the mouth, and at times destructive lesions of the eyelids and eyeball; a severe diarrhoea may hasten the fatal termination. In such cases the slightest application of force may cause the wool to separate from the skin.

Captain J. Carr (quoted by Simonds) thus describes this malignant form: "The pulse becomes increasingly rapid, the mouth dry and hot, the breath fetid, and the eyelids and even head so much swollen that the creature can scarcely be recognized. The pustules may produce malignant ulcers and render the poor animal lame or blind."

Sacco states that "impregnated ewes are certain to abort their lambs."

The mortality rate is high, varying between 25 and 50 per cent. When death takes place it is most apt to occur during the first week of the eruption.

That the disease may be conveyed through the atmosphere is evidenced by the fact that sheep that have never come in contact with infected animals, but have been kept in neighboring pens, have contracted the disease.

Youatt states of sheeppox that "if it broke out in a flock, it was almost sure to be communicated, sooner or later, to all that were within a few hundred yards of it."

The disease may also be conveyed by *inoculation*, or *ovination*, as it has been termed. Ovination has been extensively employed in order to mitigate the ravages of natural sheeppox. The disease under such circumstances commonly develops after four to eight days, and when performed with special precautions usually produces a milder malady than when contracted in the usual manner. D'Arboval records the fact that of 32,317 sheep inoculated, 32,121 took the disease, of which 31,851 recovered and 270 died. The inoculated sheep to the number of 7697 were subsequently exposed to the infection of sheeppox without any of them contracting it. Inoculation was not so successful in the hands of Simonds and of Ceely, who lost in their first experiments almost 20 per cent. of their sheep.¹

It has been stated that ovination of pregnant ewes will subsequently protect the newborn. This is denied by D'Arboval, who says that the lambs born of sheep which had been affected with the natural *clavelée* (sheeppox), or those which were inoculated during pregnancy, do not acquire an immunity thereby from the malady.

Some difference of opinion exists as to the prophylactic power of *vaccination* against *variola ovina*. D'Arboval contends that inoculation

¹ These experiments were conducted on a much smaller scale than those of D'Arboval.

of a large number of sheep with virus from the cow failed to protect them against sheeppox. Sacco, on the other hand, declares that "he has fully satisfied himself by repeated experiments of the power of vaccination to destroy the susceptibility of sheep to contract variola ovina."

Human Ovation.—Sacco inoculated about 300 children with the virus of sheeppox and claimed that the ovination protected them against smallpox. He states: "I subsequently determined to inoculate two children with ovine lymph on one arm and vaccine on the other; the vesicles were so similar in appearance that had I not marked the arms I should not have been able to distinguish the one vesicle from the other. A few days after the desiccation of the vesicles the children were inoculated with the virus of human smallpox, but no consequences, either local or general, resulted therefrom."

The successful inoculation of sheep virus in the human subject is, however, much more difficult than would appear from the above statement, inasmuch as Simonds, Ceely, and Marson all failed in similar attempts, although the two latter investigators performed no less than 250 inoculations. D'Arboval also failed in conveying ovine lymph to the human subject, for he states that he successfully vaccinated a number of children after ovination had been tried. He also remarks that efforts to communicate sheeppox by inoculation to horses, oxen, goats, deer, pigs, dogs, monkeys, rabbits, and various birds were likewise unsuccessful.

We believe the conclusion may be drawn that while the smallpox of sheep and that of man resemble each other clinically, and are doubtless closely related to one another, the two diseases are not identical. It would appear that sheeppox may at times be inoculated into the human subject, but there is no reason to believe in the intercommunicability of human and ovine variola by ordinary infection. No one has ever observed the smallpox of sheep give rise to smallpox in man, nor has the reverse route of infection ever been recorded.

Goatpox.—The existence of a primary goatpox is doubted by most authors, the view being held that this animal, which is zoologically closely related to the sheep, contracts the disease from the sheeppox. The goatpox is accompanied by high fever and a generalized eruption. The disease is extremely rare.

That the goatpox is similar in its nature to cowpox appears probable from information contained in a letter written by Prof. Heydeck to Dr. Dunning, and quoted by Baron. The letter reads: "The King ordered in September that all the children in the Foundling House should be inoculated with the goatpox, which did its effects."

Variola Equina, Horsepox, Grease or Eaux aux Jambes.—The various appellations here mentioned have been applied to a pock disease in the horse which bears a close relationship to vaccinia and variola. The term *grease*, Jenner tells us, was employed by farriers to designate this disease upon the heels of horses. It is regretted by some writers that Jenner used this term instead of variola equina, for the employment

of this name has given rise to some confusion. Lupton¹ in 1800 pointed out that the true analogy of cowpox in the horse was not the *grease* nor any form of *grease*, but a disease regarded by the neighboring farmers as widely different from it, and called by them "scratchy heel."

Loy in 1801 distinguished two forms of grease, the acute and the chronic, the former of which alone was capable of imparting the disease to the bovine of human species.

Horsepox, unlike the variolous disease in man and in sheep, does not seem to arise through the action of a volatile contagium, but practically always results from inoculation, either accidental or intended. The disease is ushered in with fever, but this in many cases is slight and often absent. The eruption exhibits a decided preference for the fetlock joints of the hind legs, perhaps because these parts are most subjected to traumatism. The eruption is in many cases limited to this region, but a more general eruption may exist either primarily or result secondarily from autoinoculation. Perhaps the not infrequent presence of lesions in the nasolabial region may be explained upon the grounds of autoinoculation. Occasionally, more particularly in certain epizootics, an extensive eruption may be present, involving the head, belly, and legs. Such profuse eruptions may be primary or may appear after the ordinary local symptoms have manifested themselves. The lesions begin as firm papules, which soon become flattened and are often umbilicated. By the eighth or ninth day there are seen pea-sized, round, notably elevated vesicles, which on rupture give exit to a viscid, yellowish fluid. The surrounding skin is reddened and tumefied. The pocks may now be transformed into superficial, slowly healing ulcers, or may be covered with crusts, which fall off from the fifteenth to the twenty-fifth day.

Jenner briefly refers to grease in the following words: "The skin of a horse is subject to an eruptive disease of a vesicular character, which vesicle contains a limpid fluid, showing itself most commonly in the heels. The legs first become œdematous, and then fissures are observed. The skin contiguous to these fissures, when actually examined, is seen studded with small vesicles surrounded by an areola. These vesicles contain the specific fluid."

It will be seen from the above description that equine and bovine variola closely resemble each other. The disease in the horse distinguishes itself from that in the cow principally by the locality of the eruption—usually the heels and the nasolabial mucous membrane, the occasional tendency to generalization of the eruption, and by attacking the male as well as the female.

The Relation of the Equine Disease to Cowpox.—Great interest attaches to this subject inasmuch as Jenner regarded *grease* as the progenitor of cowpox. Jenner informs us that in dairy counties in England it was frequently the custom for farm hands to dress the sores on horses and subsequently, without due attention to cleanliness, to

¹ Medical and Physical Journal, November, 1800, vol. iv.

milk the cows. In this manner infectious matter was carried to the teats of cows, producing the cowpox. From this source other cows and many of the dairy hands became infected.

Numerous experiments have proven the correctness of Jenner's assertion that cowpox results from inoculation with matter from the grease. Woodville took exception to this view, basing his contentions upon the negative experiments of the veterinary professor, Coleman; the latter, however, after many unsuccessful results, succeeded in producing cowpox from the grease. The horsepox has been artificially produced in the horse and other animals by inoculation. This can be done with equine lymph directly transferred from horse to horse, with equine lymph that has been successfully passed through the cow (in other words, with vaccine virus of equine origin), and finally with pure cow lymph. In horsepox produced by inoculation, the eruption, almost without exception, is limited to the site of the introduction of the lymph.

The belief entertained by Jenner, that the grease was the *invariable* source of natural cowpox, is not concurred in by most observers. There are many modern writers who are of the opinion that horsepox is nothing more than a variola or vaccinia accidentally derived from the human or bovine species. That the latter theory is correct is rendered probable in view of the fact that both cowpox and human variola may be transplanted to the horse with the production of horsepox.

Chauveau injected vaccine lymph beneath the skin and into the bloodvessels and lymphatics of colts, and produced a generalized eruption of horsepox.

Copeman remarks that in all probability Jenner was mistaken in his assumption that "grease," in the sense of horsepox, was a necessary antecedent to cowpox; but at the same time there can be little doubt that the two diseases are very closely allied, if, indeed, they be not identical."

We may assume that the two diseases have a common ancestry, without unavailingly attempting to adduce proof as to the priority of either. There is equal reason to believe that the hands of the groom may carry the infection from the cow to the horse as well as from the horse to the cow.

Human Equination.—Horsepox has been successfully inoculated into the human subject, with the production of vesicles similar to those observed in cowpox, and with the effect of conferring immunity against smallpox.

J. G. Loy¹ succeeded in transferring lymph from cases of equine variola to the teats of cows, producing in them typical cowpox. From the vesicles thus formed he inoculated children and secured beautiful vaccine lesions. He furthermore inoculated horsepox directly into the human species. We quote his description of the results: "Some grease matter, obtained from the same horse, was inserted in the arm of a child. On the third day a small degree of inflammation surrounded

¹ *Experiments on the Origin of the Cowpox*, England, 1801, pamphlet of 29 pages.

the wound. On the fourth day the inoculated place was much elevated, and a vesicle of a purple color was formed on the fifth day; on the sixth and seventh days the vesicle increased and the inflammation extended and became of a deeper color; on the same day a chilliness came on, attended with nausea and some vomiting. These were soon succeeded by increased heat, pains in the head, and a frequency of breathing; the feverish symptoms soon abated and disappeared entirely on the ninth day. On the sixth day smallpox virus was inserted into the same arm in which the matter of grease had been placed, but at a considerable distance from it. On the fourth and fifth days of the smallpox inoculation some redness appeared about the wound, and on the sixth a small vesicle. The inflammation now decreased and on the ninth day the vesicle was converted into a scab."

From this child, on the sixth day, before the smallpox virus was inserted, matter was procured and inoculated into five other children. A vesicle was produced in each case. Ten days after the insertion of the lymph the children were all inoculated with smallpox virus, but nothing developed save a little inflammation at the site of the punctures.

The Italian investigator, Sacco, in a letter written to Jenner in 1803, describes similar experiments: "A coachman came to the hospital for an eruption which he had on his hands. It was immediately recognized that he had contracted horsepox in caring for and dressing horses. I made nine inoculations (from the sores) on as many children. Three of these contracted an eruption exactly like that of vaccinia. I made other inoculations with the material from these children, and it has already been reproduced in four generations, with the same effect as the vaccine disease. I inoculated several of these individuals with smallpox, but without any effect. I also finally obtained, with the virus of grease inoculated into six other children, two lesions exactly like vaccine lesions."

Martin, of Boston, observed a case of casual horsepox in 1881, and obtained typical vaccine vesicles therefrom. He was "called to a man of about sixty, in bed with considerable headache and febrile reaction. He presented vesicular sores, two upon the right hand and one upon the nose, surrounded by areolæ, and very painful. These lesions had existed for about five or six days. The patient was employed as a groom in a horse-car stable in which were a large number of horses suffering from sore heels, and his duties obliged him to constantly handle these heels. The lesions in the groom closely resembled vaccine vesicles, and the exuding lymph was therefore collected upon ivory points and inoculated into several children and a number of heifers. In every case a typical vaccinal result was obtained. This 'stock' was continued through cows for some time." It is interesting to note that Martin discovered casual cowpox at Cohasset during the same month.

A number of other competent observers have confirmed the above experiments; so that it may be accepted that human beings can be

equinated with virus taken from the horse, and that such inoculations protect against smallpox.

Retro-equination has been successfully essayed in horses with bovine or human virus of equine origin.

Natural Vaccinia, or Cowpox in the Cow.—Cowpox of spontaneous development is occasionally discovered in members of the bovine species. The disease in such cases is designated natural cowpox in contradistinction to the affection inoculated by design. Natural cowpox is an uncommon disease; indeed, it is so rare that to each case attaches an historical interest. From each cow with spontaneous cowpox a special strain of lymph is cultivated and perpetuated, so that these first sources are most highly prized. The disease is most apt to be observed in spring and early summer, when cattle yield the most milk; while any member of the bovine family (even the bull) may be attacked, it is particularly the milch cow in which the disease is found. The eruption is never generalized, but is circumscribed to the udders or their base. The location of the lesions constitutes strong evidence that the hands of the milker are the most important factor in the transmission of the disease. When the disease once appears in the herd, it spreads with considerable rapidity from one cow to another.

The disease is described by the older writers as beginning with the formation of vesicles, although these are doubtless preceded by a brief stage of papulation. The vesicles are of a bluish color and situated upon a reddened and swollen base. If rupture takes place the vesicle is converted into a superficial ulcer with irregular edges, which may heal with great slowness. Desiccation begins about the twelfth day. During the suppurative stage there is usually some elevation of temperature, loss of appetite, and a lessening of the milk secretion. Natural cowpox frequently exhibits a succession of lesions, coming out in crops, in this respect differing from the inoculated disease. After the termination of the disease depressed scars are left which may often be distinguished for years.

Cowpox, both the natural and inoculated form, confers a permanent immunity against a second attack. No authentic case has been reported in which a cow has twice suffered from the disease.

Casual or Accidental Cowpox in Man.—It was from observation of cases of casual cowpox in dairy attendants that Jenner first conceived the theory of vaccination. These infections result from the contact of fluid from the lesions on the cow's teats with abrasions upon the hands of the milkers; one, two, or more lesions are produced, according to the number of excoriations present. Upon areas of reddened skin there soon spring up vesicles or blebs, which are of a bluish color, rounded, flat, and depressed in the centre. These contain a lymph fluid which later becomes purulent. The surrounding skin becomes reddened and tumefied, owing to the development of an erysipelatoid areola about each lesion. The neighboring lymphatic glands become swollen and painful, and the patient becomes feverish. In severe cases the illness may be sufficiently pronounced to enforce confinement to bed for a few

days. In a few days, however, there is an abatement of the local inflammatory disturbance, and of the constitutional symptoms, and the pustules either become encrusted or form ulcers which gradually heal by granulation. In casual cowpox the local and constitutional symptoms are more severe than when the disease is intentionally inoculated, probably because in the latter case special precautions are observed.

Apepox.—The monkey appears to be susceptible both to smallpox and vaccinia. Zuelzer claims that he produced true variola in monkeys by inoculation with the blood and crusts of human variola. Cope-man has also succeeded in inoculating monkeys with the fluid from lesions of human smallpox. More recently successful inoculations have been carried out by Magrath and Brinckerhoff.¹ Usually the resulting eruption is limited to the sites of inoculation, but occasionally a generalized outbreak occurs which may cover the entire surface of the body. Inoculated smallpox in the monkey is, however, seldom fatal. The monkey may be rendered insusceptible to smallpox by previous vaccination.

It is claimed that in the tropics apes sometimes die in large numbers of natural smallpox.

Anderson, of Glasgow, states that while smallpox was raging with great violence at St. Jago, on the west coast of New Grenada, monkeys were attacked with the disease in the forests near David, sixty or seventy miles away. Dying and dead monkeys were seen on the ground covered with perfect pustules of smallpox, and several ill monkeys were seen on the trees, moving about in a sickly manner. In the course of a fortnight one-half of the inhabitants of the town of David were stricken with smallpox.²

Smallpox in the Camel.—In the province of Lus, in Beloochistan, the camels are said to be subject to a disease called "Photoshootur," or the smallpox of camels. This disease is said to be communicable to the camel milkers, and is alleged to protect them against smallpox.³

¹ Journal of Medical Research, February, 1904.

² Quoted by William Aitken, Practice of Medicine, 1868, p. 258.

³ Quoted by Seaton, Indian Journal of Medical Sciences, October, 1839.

CHAPTER IV.

SMALLPOX.

Synonyms.—Latin, *Variola*; French, *La Petite Vérole*; German, *Blattern*, or *Pocken*; Italian, *Vajuola*.

Definition.—Smallpox is an acute infectious disease characterized by an initial fever of about three days' duration, succeeded by an eruption passing through the stages of papule, vesicle, and pustule, ending in incrustation and leaving pits or scars, the fever either intermitting or remitting in the papular stage and increasing in the pustular stage.

Derivation of Name.—Some difference of opinion exists as to the derivation of the term *variola*. It is alleged by some that it was coined by the monks during the Middle Ages, and that it is the diminutive form of the Latin word *Varus* (a papule, pimple, or tubercle), a word found in Pliny. Other writers, however, believe it to be derived from the word *varius*, which means spotted or variegated.

The Saxon equivalent *pocca*, meaning a bag or pouch, has given rise to the English *pock* and the German *Pocken*. Syphilis appeared in Europe about 1498 and caused some confusion of nomenclature, so that it became necessary to prefix the adjective *small* to the term *pock*, or *pox*, in order to distinguish it from the great pox, or syphilis. The same change was made in French phraseology; so that at the present day, *variola* is designated *smallpox*, or *la petite vérole*, and syphilis the *pox*, or *la vérole*.

History.—It is claimed by some writers that the antiquity of smallpox dates back to the time of the Tsche-u dynasty in China, at a period not less remote than a thousand years before the Christian era. It is stated that temples were erected in honor of the disease, and the goddess of smallpox was thus glorified. Inoculation, or "sowing the smallpox," it would appear was practised in China at a very early period, the result being crudely attained by thrusting crusts into the nostrils.

Tradition has it also that smallpox existed among the Brahmin caste of India from time immemorial. Descriptions in some of the ancient sacred writings of spotted and pustular skin diseases are alleged to relate to smallpox. Like the Chinese, the inhabitants of Hindoostan are also said to have worshipped at smallpox shrines and to have offered sacrifices to the presiding goddess to grant them protection.

That the Greek physicians were acquainted with smallpox is open to most serious doubt. Some authors have labored diligently to prove that the great vesicular and pustular eruptions and "anthrakes" which Hippocrates (460–377 B.C.) speaks of relate to smallpox. While the descriptions are somewhat suggestive of this disease, they are far from constituting satisfactory evidence.

The first writings of the Roman period bearing upon the subject are those of the Jewish philosopher of Alexandria, Philo, who lived in the first century. His description of the Egyptian plague¹ might with greater reason be assumed to refer to smallpox than the writings of Hippocrates: "From the great suffering, natural to the fermentation of festers so extensive, their bodies were tortured and their minds filled with horror. The lesions thrown out soon merged into extensive blisters filled with pus, as if the parts had been burned. It extended over the whole body from head to foot." This description is, as Haeser contends, strongly suggestive of confluent smallpox.

Haeser² concludes, from a study of the Greek and Roman writings, "that knowledge of smallpox among the ancient Greeks and Romans probably existed, although we cannot with absolute certainty either affirm or deny this assertion."

The word "variola" is first mentioned by Bishop Marius, of Lausanne, who employed the term (*et variola Italiam Galliamque afflixit*) in 570 A.D. in describing a devastating epidemic that swept through Italy and France. The same epidemic was doubtless referred to by Bishop Gregory, of Tours, who, in 582, under the name of "lues cum vesicis," described a disease characterized at the beginning by high fever, vomiting, and "back pains," followed by the appearance of a painful eruption of hard, white vesicles, which occurred most conspicuously over the face, hands, and feet; the vesicles became pustules, and in many cases death occurred on the twelfth or fourteenth day.

Procopius, in a chapter "De Bello Persico" (lib. ii., cap. 27), described a dreadful pestilence which began in Pelusium, Egypt, in the year 544. It was accompanied by buboes and carbuncles (suggesting bubonic plague), but was widespread, raged independent of season, spared neither age nor sex, attacked pregnant women severely, and was a new disease but little understood by physicians.

A short time afterward, unequivocal traces of smallpox are met with in countries bordering on the Red Sea; for we read of caliphs and caliphs' daughters being pitted and having white spots in their eyes.

In 569 A.D. smallpox appears to have broken out in virulent form in the Abyssinian army of Abraha, which was besieging Mecca. The soldiers were decimated by the pestilence, necessitating the raising of the siege.

Reference to a lost treatise on smallpox (seventh century) by an Alexandrian physician, Aaron, is found in the writings of Rhazes.

Edwardes³ says: "The first clear description of smallpox by a physician, which has come down to us, is by Isaac, the Jew, who lived in the ninth century. A manuscript latin translation of his work is in the town library of Mainz (*Isaaci Israeliti. . . . opera omnia*)."

The most scientific and comprehensive description of smallpox handed down from these times, however, is from the pen of Rhazes, who wrote

¹ Vita Moses, 1, C. 22, Ed. Tauchnitz (Bonn, 1838), tome iii. p. 151.

² Geschichte der Epidemischen Krankheiten, Jena, 1865, p. 27.

³ Smallpox and Vaccination in Europe, 1902.

in about 910. The Bagdad physician was a prolific writer and a close observer, and has been called "the Arabian Galen." The following quotations are of interest:

"As soon as the symptoms of smallpox appear we must take especial care of the eyes, and then of the throat, and afterward of the nose, ears, and joints. . . . If a severe pain arises in the soles of the feet, then take care to anoint them with tepid oil, and foment them with hot water and cotton, . . . for these and the like things soften and relax the skin, and thus facilitate the eruption of the pustules and lessen the pain."

"All those pustules that are very large should be pricked, and the fluid that drops from them be soaked up with a soft, clean rag in which there is nothing that may hurt or excoriate the skin."

"When the desiccation of the pustules is effected, and scabs and dry eschars still remain upon the body, examine them well, and upon those that are thin and perfectly dry, and under which there is no moisture, drop warm oil of sesamum every now and then, until they are softened and fall off."

". . . and in order to efface the pock holes, and render them even with the surface of the body, let the patient endeavor to grow fat and fleshy, and use the bath frequently and have the body well rubbed."

The above therapeutic suggestions might be incorporated in a modern treatise on smallpox with but little revision. Rhazes credits Galen with a knowledge of the disease, and also quotes from Hippocrates, Aaron, and Masawaih. The last-named writer is cited as saying: ". . . Your first care should be directed to the eye, for which you should use a collyrium made of sumach and rose-water, in order to prevent any pustules from coming out in it."

Avicenna (980-1037), an Arabian physician, was the first to distinguish smallpox from measles. In the *Canon Medicinæ* he states of measles "that in it more tears flow." He also conceded the possibility of second attacks of smallpox.

Franciscus de Pedemontium (1330) referred to red coverings and warm air as tending to expel the pustules to the surface, for, "according to Avicenna the sight of red bodies moves the blood."

Constantinus Africanus (1075 A.D.), a Carthaginian, who lectured at Salerno, the first European medical school, closely followed, as did his contemporaries, the Arabian doctrines. He restricted the term variola, which was at that time loosely employed, to smallpox.

A tenth century Anglo-Saxon manuscript, in the Harleian collection in the British Museum, contains an exorcism and prayer in which the following words appear: ". . . Geskyldath me vid de lathan Poccas," which, rendered into modern English, reads: "Shield me against the hideous pocks."

A Cottonian manuscript, evidently written in the eleventh century, contains a prayer to Saint Nicaise, who had the smallpox, and whose name was to be worn in an amulet to grant protection.

The term pocca, which was the Anglo-Saxon equivalent of variola,

is first encountered in a tenth-century leech-book of the physician Bald. The death of Baldwin (961), son of the Earl of Flanders, from "variolas sive poccas" is set forth in the *Bertinian Chronicle*.

Smallpox is supposed to have invaded England between the tenth and thirteenth centuries. Holinshed, describing an epidemic in the reign of Edward III., writes: "Also many died of *small pokkes*, both men, women, and children." According to Hirsch, Iceland suffered from smallpox in 1306, having received the infection from Denmark.

John of Gaddesden, physician of Edward II. and author of *Rosa Anglica*, followed the Arabian treatment of surrounding the patient with red bed-clothing, hangings, etc. He acquired a great reputation, but, according to Watson, was a "very sad knave."

During the epidemic of 1694, Queen Mary, the wife of William III., died at the age of thirty-three of hemorrhagic smallpox. Lord Macaulay, writing of the ravages of this disease, says:

"That disease, over which science has achieved a succession of glorious and beneficent victories, was then the most terrible of all ministers of death. The havoc of the plague had been far more rapid; but the plague had visited our shores only once or twice within living memory; and the smallpox was always present, filling the church-yards with corpses, tormenting with constant fears all whom it had not yet stricken, leaving on those whose lives it spared the hideous traces of its power, turning the babe into a changeling at which the mother shuddered, and making the eyes and cheeks of a betrothed maiden objects of horror to the lover."

Smallpox was treated in diverse and various manners in different periods. In 1640 the hot or sweating treatment, by which the peccant humors were to be expelled, was in vogue. Diemerbroeck, a Dutch physician and professor, was an advocate of this method. Gregory remarks that when Sydenham began his medical reform, in 1667, "he had an Augean stable to cleanse." The "English Hippocrates," however, was equal to the task, and succeeded in completely changing the practice with regard to smallpox. He insisted upon fresh air, and substituted the cooling for the sweating treatment. He also described the disease admirably, and was the first to trenchantly distinguish between measles and smallpox. Boerhaave (1668-1738) was a warm admirer of Sydenham. He deserves the credit of having maintained that smallpox was contagious and due to a specific miasm.

Smallpox in America.—It is said that smallpox reached Mexico in 1518, having been brought by a negro slave who accompanied the troops of Cortez from Cuba. According to Toribio it swept the country, destroying the lives of three and a half millions of people. De la Condamine states that whole tribes of Indians were exterminated, and in some places no one was left to bury the dead. The disease then reappeared at regular intervals of seventeen or eighteen years. In 1633 the Indians of Massachusetts were attacked by smallpox and slain by the thousands. The disease first appeared in Boston in 1649.

Referring to the importation of smallpox into America, Gregory

humorously remarks: "If America gave us, as people confidently say it did, the great pox, we have more than returned the compliment by introducing to her acquaintance the smallpox."

In 1707 smallpox reached Iceland, destroying the lives of 16,000 people, almost one-third of the population of the island.

Period of Inoculation.—Inoculation was first practised in Constantinople about the year 1674. Dr. Timoni (1714), Dr. Kennedy (1715), and Dr. Pylarini (1716) wrote on the subject of inoculation, but the profession in England ignored the publications. It remained for the charming and accomplished Lady Mary Wortley Montague, wife of the British Ambassador to Turkey, to introduce inoculation to the European world. The now famous letter to her friend, Miss Sarah Chiswell, written in 1717, is here appended:

" . . . Apropos of distempers, I am going to tell you a thing that will make you wish yourself here. The smallpox, so fatal and so general amongst us, is here entirely harmless by the invention of engrafting, which is the term they give it. There is a set of old women who make it their business to perform the operation, every autumn in the month of September, when the great heat is abated. People send to each other to know if any of their family has a mind to have the smallpox: they make parties for this purpose, and when they are met (commonly fifteen or sixteen together) the old woman comes in with a nutshell of the best sort of smallpox, and asks what vein you please to have opened. She immediately rips open that you offer to her with a large needle (which gives no more pain than a common scratch), and puts into the vein as much matter as can lie upon the head of her needle, and after that binds up the little wound with a hollow bit of shell, and in this manner opens four or five veins. . . . The children or young patients play together all the rest of the day and are in perfect health to the eighth. Then the fever begins to seize them, and they keep their beds two days, very seldom three. They have very rarely above twenty or thirty on their faces (*sic*), which never mark, and in eight days' time they are as well as before their illness. Where they are wounded there remain running sores during the distemper, which I do not doubt is a great relief to it. Every year thousands undergo this operation, and the French Ambassador says, pleasantly, that they take the smallpox here by way of diversion, as they take the waters in other countries. There is no example of anyone that has died of it, and you may believe that I am well satisfied of the safety of this experiment, since I intend to try it on my dear little son. I am patriot enough to take pains to bring this useful invention into fashion in England, and I should not fail to write to some of our doctors very particularly about it, if I knew any one of them that I thought had virtue enough to destroy such a considerable branch of their revenue for the good of mankind. But that distemper is too beneficial to them, not to expose to all their resentment the hardy wight that should undertake to put an end to it. Perhaps if I live to return, I may, however, have courage to war upon them. Upon this occasion admire the heroism in the heart of

"Your friend," etc.

The daughter of Lady Montague was the first person ever inoculated in England (1727), although her son had previously been inoculated in Constantinople. In the following year, after six condemned criminals had been successfully inoculated, the two daughters of the Princess of Wales submitted to the new process.

During the first ten years of its career inoculation met with great opposition. Later it became more firmly established, and was extensively practised in England up to 1800. It never, however, became popular on the Continent. The average death rate from inoculation was about one in three hundred cases, although it often rose above this. In 1798 Jenner announced his discovery of vaccination. In 1808 the inoculation of out-door patients was discontinued at the London Smallpox Hospital, and fourteen years later inoculation of in-door patients was abandoned. In 1843 Gregory wrote: "In 1840 the practice of inoculation, the introduction of which has conferred immortality on

the name of Lady Montague, which had been sanctioned by the College of Physicians, which had saved the lives of many kings, queens, and princes, and of thousands of their subjects during the greater part of the preceding century, was declared illegal by the English Parliament, and all offenders were sent to prison with a good chance of the treadmill. . . . Such are the reverses of fortune to which all sublunary things are doomed."

Inoculation was first practised in America in 1721. It was introduced into this country, at the suggestion of the Rev. Cotton Mather, by Dr. Zabdiel Boylston, of Boston, who first inoculated his only son and then two negro servants. Before the practice was generally accepted, however, it was necessary to overcome here, as in England, much violent opposition.

The principal advantage claimed for inoculation was that smallpox thus produced was much milder in type than when the infection was received in the natural way; while the death rate from smallpox was one out of every three or four persons attacked, it was, at the highest from the inoculated disease, not greater than one out of fifty, and sometimes as low as one out of three hundred, the average death rate being somewhere between the two. Not only the number of deaths, but the marred visages of persons in every community, testified to the frequency of smallpox before the days of inoculation. Indeed, it was so prevalent in the Middle Ages as to lead to the common saying that "*from smallpox and love but few remain free.*" The disadvantage of inoculation was that smallpox produced in this manner, although milder in type, was just as contagious as when contracted naturally; hence inoculation had the effect of keeping the disease almost constantly in existence.

Prevalence of Smallpox in the Prevaccination Days.—Smallpox was so universal a disease that Ben Jonson wrote of it:

"Envious and foul disease, could there not be
One beauty in an age and free from thee?"

Smallpox was mainly a disease of children in former times, and the adult population consisted for the most part of the survivors from an attack in childhood, therefore permanently protected. The disease was regarded as universal or almost universal.

According to Dr. Lettsom, most children in London had smallpox before the seventh year.

Juncker estimated that 400,000 smallpox deaths occurred yearly in Europe on an average, and that five-sixths of mankind were attacked. Many writers were of the opinion that every one was attacked sooner or later. King Frederick William III. of Prussia, in a dispatch dated October 31, 1803, states that smallpox caused on an average 40,000 deaths yearly in Prussia.¹

That smallpox did not respect royalty is evidenced by the formidable list of kings, queens, and princes who died of the disease: William II of Orange, Emperor Joseph I. of Austria, Louis XV. of France, two

¹ The above statements are quoted from Edwardes' *Smallpox and Vaccination in Europe*, 1902.

children of Charles I. of England, a son of James II. of England, his daughter Queen Mary, and her uncle, the Duke of Gloucester; the son of Louis XIV.; Louis, Duke of Burgundy; the dauphin, his wife, and their son, the Duc de Bretagne; Peter II., Emperor of Russia; Henry, Prince of Prussia; the last Elector of Bavaria, two German empresses, six Austrian archdukes and archduchesses, an Elector of Saxony, and the Queen of Sweden (1741.) The following were attacked with the disease, but recovered: Queen Anne of England, Peter III. of Russia, Louis XIV. of France, William of Orange (afterward William III.), and Queen Maria Theresa of Austria. George Washington was "strongly attacked by the smallpox" during his early manhood, while on a visit to the West Indies.

THE ETIOLOGY OF SMALLPOX.

That smallpox may prevail in the frigid climes of Greenland and in the torrid regions of Africa is evidence of the fact that conditions of soil or climate exert but little influence over the disease. Practically no civilized country on the globe has been exempt from the ravages of smallpox. It follows, like other transmissible diseases, the channels of trade and human intercourse. When the contagium of the disease is brought to an unprotected community, there the malady takes root and spreads.

Susceptibility to smallpox is almost universal; but few persons can boast of natural immunity from this disease. Yet this individual peculiarity is occasionally encountered, as may be seen by reference to the history of the disease during the prevaccination period. Persons have been known to go through life constantly exposed to the infection without suffering from any manifestation of smallpox. It is said that Morgagni, Boerhaave, and Diemerbroeck enjoyed this privilege. It is not impossible that such immunity may have resulted from a mild attack of smallpox, from which such persons may have suffered *in utero*, even without their mothers having presented any manifestations of the disease.

Instances are recorded in which persons have resisted the infection when exposed in the usual manner, but have yielded to the disease by inoculation later in life. Gregory gives an example of this kind in the case of a lady who brought up a large family of children, many of whom she nursed through smallpox without receiving the infection herself, but at the age of eighty-three she took the disease by inoculation. While but few are naturally insusceptible to smallpox, through the agency of vaccination, individual susceptibility at the present day, is greatly changed; absolute immunity, indeed, is enjoyed by the greater part of the population.

Instances are met with, under rare circumstances, of apparently healthy persons resisting the infection of smallpox at one time and yielding to it at another. We will relate a case in point: In 1874 a colored man of thirty years came under our care suffering from con-

fluent variola. He stated that vaccination had been performed at different times during his life, but never successfully: In 1871 he belonged to the crew of a sailing vessel in which several cases of smallpox occurred, and his duties required him to frequently come in contact with those who were ill, yet he did not take the disease. He was vaccinated at that time, but, as before, without result. When he fell ill with variola three years later he was unable to account for the source of the infection. The attack proved fatal.

In the days when inoculation was extensively practised it was noticed that some persons exhibited a temporary insusceptibility to the infection. Gregory informs us that Woodville found one out of every sixty children, and one out of twenty adults, to be temporarily insusceptible to inoculation. Experience demonstrates that the susceptibility to smallpox may at one time be diminished and at another greatly increased.

The existence of acute and chronic infectious diseases is said by some writers to temporarily lessen the susceptibility to the infection of variola. Curschmann asserts "that for an individual suffering from scarlet fever, measles, or typhoid fever, there is during the entire duration of the affection only a very slight susceptibility to an attack of variola." He observed in the hospital at Mayence (where the smallpox building was near the general wards) that variolous infections never took place during the course of the typhoid process. A considerable number of typhoid convalescents, however, were attacked after their temperatures had become permanently normal. He was led to this conclusion from the fact that the interval between the time of the subsidence of the fever and the beginning of the initial stage of variola corresponded to the longest period of incubation that is encountered—namely, fourteen to nineteen days. There is no doubt, however, that the variolous infection does frequently occur during the existence of an acute disease, only the incubation period in such cases is often greatly prolonged. Smallpox has been known to exist with the acute exanthemata, particularly scarlet fever and measles. We have seen unprotected children, while suffering from measles in its most acute stage, exposed not longer than two minutes to the infection of variola, sicken with the disease after the usual incubation period. We have also observed this sequence of events to develop in connection with a diphtheria patient. In at least a half-dozen instances we have noted the coexistence of smallpox and scarlet fever. Chronic infectious maladies, such as syphilis and tuberculosis, not infrequently exist in individuals who are attacked by smallpox.

Recurrent Smallpox (Second Attacks).—The susceptibility to smallpox is removed by vaccination, but frequently reappears to a greater or less degree in a variable period of time. So also one attack of smallpox does not invariably protect the individual for the remainder of his life against a future attack. It is undoubtedly the rule that a person does not suffer from the disease more than once, but well-authenticated cases of second attacks are recorded. Indeed, some writers allege that the predisposition to smallpox in some persons is so strongly marked as to render them susceptible to the infection more than twice, even as

often as five or six times. The authenticity of reported cases of this kind, however, is not to be taken for granted, but accepted with extreme caution, as there are many sources of error.

As to the frequency of secondary or recurrent smallpox, there is some difference of opinion on the part of authors. Many of the cases reported in the olden times were doubtless based upon an error of diagnosis, for the second attacks appear to have occurred almost exclusively in children. Some of the more practical writers of the early part of the last century hesitated very long before believing that it was possible for the disease to recur. The infrequency of such cases was accurately observed during the time inoculation was in vogue.

Jenner, who closely studied casual and inoculated smallpox for more than thirty years, was very positive in his views as to the permanency of the protection which one attack of the disease conferred, and it was doubtless his positive convictions on this point that led him to announce his oversanguine belief in the permanency of the vaccine influence.

Gregory, who enjoyed unusual opportunities for studying variola, was very incredulous on the subject of recurrence of the disease. Most of the reported cases which he was called upon to examine he found incorrectly reported. Echthyma, pustular syphilis, and particularly varicella, he states were fruitful sources of error. But few patients claiming to have had smallpox previously came under his care as physician to the Smallpox Hospital of London for more than twenty years, and of these few only a very small fraction could stand the test of rigid scrutiny. Koch states that in the great epidemic of 1871-72, among 12,000 cases of smallpox in South Germany, no second attack occurred.

Marson is responsible for the statement that during the one hundred and nineteen years since the founding of the London Smallpox Hospital, there is no record of a patient having been admitted twice, suffering from smallpox. He reports, however, the following interesting instance of recurrent smallpox: "An Irishman, the son of a medical officer of the army, who had been vaccinated in infancy by his father, and who had a large cicatrix remaining from the vaccination, and who was attended by his father for smallpox in early life and bore decided pits of the disease, in 1844, at twenty-three years of age, was admitted to the Smallpox Hospital with severe confluent smallpox, of which he died." Marson believes that exposure for a time to a great change of climate, either hot or cold, seems to predispose the constitution to receive a second attack of smallpox.

It is said that Grossheim observed a light form of variola in a patient three months after the first attack, but this peculiar case was the only instance of recurrence which he noted among 22,641 in the German Military Hospitals.

In regard to the historic case of Louis XV., Gregory has the following to say: "The most remarkable case of recurrent smallpox on record is that of Louis XV., King of France, who died of it in the year 1774, at the age of sixty-four, after having, as it is alleged, undergone that

disease casually in 1724, when he was fourteen years of age. I have been at some pains to investigate this case, which created a great sensation at the time, has been quoted over and over again, and to which great importance has been attached. After careful inquiry into dates, the character of the incubative stage, and the course of the eruption, I convinced myself that his Majesty never had smallpox in early life, and that the primary attack was varicella."

We have seen in the Municipal Hospital a number of patients who claimed to have had smallpox previously, but only a very few were able to show anything like characteristic pitting; and all of those who did show such evidences of a previous attack had the disease the second time in the mildest possible form—so mild indeed, in some instances, as to be scarcely recognizable, the eruption being either arrested in the papular or in the vesicular stage. We have never seen an unmodified or even a severe case of smallpox occur in a person who was deeply and characteristically pitted from a previous attack.

Quite recently two cases of undoubted second attacks have come under our observation: one was a woman, aged twenty-nine years, who had a severe attack of smallpox at the age of one and a half years. The patient's face was fearfully scarred and seamed. The second attack was extremely mild, there being but two hundred modified lesions upon the entire cutaneous surface.

The second case was a man, aged fifty years, who had his first attack in Scotland at the age of three years; at this time five of his brothers died of the disease. The patient presented a number of superficial pits about the face. The second attack was accompanied by a fairly abundant eruption, but the lesions were distinctly modified. He had never been vaccinated.

The evidence relied upon to prove the occurrence of second attacks is usually obtained from patients themselves, inasmuch as it is exceedingly rare for a physician to observe two distinct attacks of smallpox in the same individual. During the past thirty-four years, in which period more than 9000 cases of smallpox have been treated in the Philadelphia Municipal Hospital, no person has been twice admitted suffering from the disease. In view of all that has been said, it is probable that second attacks of smallpox are much rarer than is generally supposed.

Age.—Age cannot be said to influence the predisposition to the disease, as it is naturally present at all periods of life, from earliest infancy to extreme old age. If aged persons are found less susceptible at all, it is because of the prophylactic power of vaccination. While nursing infants under six months old commonly resist the infection of measles and scarlet fever, they are nearly always susceptible to the infection of smallpox. Even the *fœtus in utero* is not exempt from the danger of an attack when a pregnant woman suffers from the disease. The variolous process in such a patient is exceedingly likely to excite abortion or premature delivery, and the *fœtus*, or child, may show evidence of the disease in the form of an eruption. Such evidence has

been observed as early as the fourth month of fetal life; we have ourselves seen a sparse eruption in the vesicular stage upon a foetus expelled at four months. We can also recall several instances of children born at or near term with the smallpox exanthem present; in one case it had advanced to the pustular stage and the child was born dead. In another case the child was born at eight months, with the variolous eruption just appearing, and died when the pustular stage was reached. It is an acknowledged fact that a woman, though personally immune, may give birth to a child suffering from smallpox; it is not improbable in such cases that the mother has passed through a *variola sine exanthemate*.

Sex.—The predisposition to smallpox is certainly not influenced by sex. Of course in every epidemic a larger number of male patients is received into smallpox hospitals than females. This is manifestly due to the fact that men are by reason of their daily occupation exposed to a greater extent to the infection.

During the last epidemic (1901-04) quite a large number of motormen and conductors employed on the street railway were admitted into the hospital. Women, on the contrary, as a result of the greater amount of time spent in-doors, are less subjected to contact with infected individuals. Of 7204 cases of smallpox treated up to 1903, in the Philadelphia Municipal Hospital, 4598 were males and 2606 were females. Under the same conditions, however, males and females are equally susceptible to the disease.

Race.—There is some difference of opinion concerning the influence of race upon susceptibility to smallpox. Most authors agree that the predisposition to *variola* is more marked among the dark-skinned peoples, particularly the negro race. There is no doubt that when smallpox prevails epidemically in this country the proportion of deaths to cases is greater among the negro than among the white race; but this we believe is owing to the fact that there is greater neglect of vaccination among the former. In our experience the unvaccinated cases of each race have perished in about the same proportion.

The aboriginal races appear to receive smallpox in a most virulent form and with fearful mortality. When smallpox first gained entrance into Mexico it spread like wild-fire, exterminating tribes to such an extent that frequently not sufficient survivors were left to bury the dead. Smallpox has also proven itself frightfully fatal among the Indian tribes of North America. In Quito one hundred thousand natives were destroyed.

Season.—Rhazes, the Arabian physician, who wrote in 900 A.D., says: "I am to mention the seasons of the year in which the smallpox is most prevalent, which are the latter end of the autumn and the beginning of the spring, and when in the summer there are great and frequent rains with continued south winds, and when the winter is warm and the winds southerly."

Sydenham said that when a smallpox epidemic is mild it begins about the vernal equinox (March 25th); but when of an extended and

dangerous kind it begins in the month of January. These generalizations are scarcely borne out by the history of smallpox visitations.

In England the smallpox appears to be most prevalent during the first six months of the year; according to Parkes,¹ the average London mortality from smallpox, from observations covering a long period of years, is greatest during the first six months of the year, rising to a maximum toward the end of May and falling through June, until it descends to the mean line, where it fluctuates during the last six months, to rise again in December or January.

In Philadelphia, smallpox during epidemic prevalence almost invariably increases in the fall of the year, beginning with the month of September or October. The number of cases then steadily rises, reaching the maximum during the months of December, January, and February, and then declining month by month until July and August, when the minimal incidence is reached.

While in temperate climates smallpox is essentially a *cold-weather disease*, the reverse is said to be true in tropical countries. The malady in such localities is alleged to be at its worst in the hot months and to improve during the cooler season.

The following tables indicate the monthly number of smallpox patients reported during the three large epidemics that have occurred in Philadelphia in the last half century:

											1871.	1872.
January											13	3180
February											6	1794
March											4	1247
April											8	587
May											9	401
June											11	208
July											15	66
August											58	30
September											111	13
October											1628	18
November											2944	11
December											3307	10
											8114	7515
											<hr/>	
Total											15,629	

	1880.	1881.	1882.	1883.	1884.	1885.
January	47	885	321	152	30	3
February	78	711	284	131	25	1
March	39	575	198	91	21	0
April	25	658	150	76	31	3
May	28	523	106	60	23	5
June	32	406	64	45	20	2
July	30	241	36	34	6	0
August	96	155	18	45	7	0
September	75	208	30	57	5	0
October	301	186	43	27	2	0
November	382	224	47	35	6	0
December	719	386	127	37	11	0
	<hr/>	<hr/>	<hr/>	<hr/>	<hr/>	<hr/>
	1866	5108	1424	790	187	14
	<hr/>					
Total	9389					

¹ Hygiene and Public Health, London, 1901.

	1901.	1902.	1903.	1904.
January	1	433	126	317
February	1	314	126	148
March	5	186	136	133
April	17	111	68	100
May	10	84	125	85
June	9	54	151	17
July	14	47	137	2
August	52	12	85	2
September	116	15	42	0
October	247	17	93	3
November	304	11	242	8
December	384	58	365	2
Total	1160	1342	1695	817
5014				

The above tables show a remarkable uniformity in the rise, culmination, and decline by month of the three epidemics. In all three the epidemic actually began in August and continued to increase throughout the autumn, reaching a culmination in December and January. A gradual decline then occurred during the spring, falling to the lowest level during the summer months.

It would appear from a study of these three visitations that the maximum intensity of epidemics in this city is reached during the winter months of the first year, particularly December and January. When the epidemic extends throughout several winters, while the highest level of each year is reached during the cold season, there is, as a rule, a gradual decline from winter to winter until the epidemic dies out.

This is well illustrated in the epidemic beginning in 1880. The epidemic beginning in 1901 is, however, an exception to this generalization. During the winter of 1902-03 it looked as if the epidemic was dying out, but during the following winter (1903-04) it acquired renewed force and almost equalled, as regards the number of persons attacked, its extent in the winter of 1901-02. Indeed, during the calendar year of 1903 there were actually more cases of smallpox in the city than during the preceding years.

In the visitation of 1871-72 the force of the epidemic was expended during the year from August, 1871, to August, 1872, when the disease was practically exterminated. Of the 15,629 cases which occurred in the two years, 15,476 developed from August to August.

In the epidemic which began in 1880 and continued for four or five years, of the total number of 9389 cases, 5502 occurred during the first year beginning with August.

Even in the epidemic beginning in 1901, which exhibited a recrudescence in 1903, the largest number of cases (2332) developed within the year from August, 1901, to August, 1902.

Influence of Atmospheric Conditions.—Moore says: "It would appear that the critical mean temperature in regard to smallpox is 50° F. When the mean temperature falls below that value, the disease spreads; when it rises above it, the disease wanes. The explanation is no doubt to be found in the fact that defective ventilation, overcrowding, and de-

ficient nutrition wait upon cold weather, and these are the most powerful predisposing causes of smallpox no less than of typhus."

Ballard,¹ commenting on the London epidemic of 1870-71 wrote: "There is some reason for believing that the variations of the epidemic (of smallpox) from week to week are influenced to a certain extent by atmospheric conditions and more especially temperature."

Mr. F. W. Alexander,² Medical Officer of Health of the borough of Poplar, from observations made during the epidemic of 1901-02, concluded that the meteorological conditions which appeared to favor the spread of smallpox were:

(1) Absence of sunshine; (2) presence of the sun above the horizon for less than eighty hours a week—*i. e.*, less than eleven hours per day; (3) temperature of the air below 50° F.; and (4) humidity above 75° (the saturation point being taken as 100°).

The Infection of Smallpox.—No one would deny at the present day that smallpox is due to a specific micro-organism. There is, furthermore, no doubt that the disease is spread by means of this organism, which is reproduced in every patient. A small quantity of the fluid from a pustule inoculated into an unprotected person gives rise to the disease; this is conclusive proof of the fact that the germ is resident in the pustules. It is also present in the exhalations from the patient and in the blood. Zülzer proved that it is contained in the blood by successfully inoculating a monkey with blood taken from a smallpox patient. It would appear from the experiments of the older writers that the physiological secretions and excretions, the saliva, sputum, urine, feces, etc., are not in themselves infectious; when, however, they become contaminated with particles derived from the skin and mucous-membrane lesions, they doubtless acquire an infectiousness.

The contagium emitted by a patient is most intense in his immediate vicinity, but it may be transported in an active state for some distance by the atmosphere. If a susceptible person should enter a poorly ventilated small apartment containing one or more severe cases of smallpox, infection would almost certainly occur, while if the apartment were large and well ventilated and the cases few and mild, the risk of infection would be diminished; if he should approach equally near the same patient in the open air, the risk would be still less.

Infectious Period of Smallpox.—Smallpox is undoubtedly infectious in all stages characterized by symptoms. It is alleged by some that the disease is even infectious during the period of incubation, but we think there is very little reason to believe that such is the case. It is possible, however, that the blood of an individual at this stage might convey the infection if it were introduced into the system of a susceptible person.

Schafer, quoted by Curschmann, reports an interesting case in this connection: "In the Charité Hospital of Berlin small pieces of skin were taken for transplantation upon other individuals from the ampu-

¹ Medical Times and Gazette, March 11, 1871.

² Abstract in Lancet, October 4, 1902.

tated arm of a person who, before and at the time of the amputation, did not manifest the slightest symptoms of general disease. Several hours after the amputation the patient was attacked with violent fever, followed two days later by the eruption of smallpox. One of the individuals upon whom the transplanted skin had been placed was attacked by variola on the sixth day after the operation. The three others remained exempt.

The disease is least infectious during the initial stage and most highly so during the suppurative and early period of the desiccative stages. The scabs are unquestionably infectious, and as long as these remain on the skin the patient should be regarded as dangerous to the community. Apart from the experience of modern observers, evidence of the infectiousness of the crusts is found in the ancient custom in vogue among the Chinese of inoculating smallpox by inserting the crusts in the nose.

Even after death the body retains the power of transmitting the contagium. This fact has been demonstrated more than once where public funerals have not been interdicted, and where bodies of persons who have died of smallpox have by accident found their way into dissecting rooms. It is said that a corpse may retain the infection in a condition to transmit the disease for an indefinite period—even for the almost incredible period of several years.¹

Austin Flint records an interesting case in which the disease was spread by a cadaver:

“During the winter of 1848–49, a young man, a member of the Medical Class of the New York University, died suddenly and unexpectedly in the night under the care of a physician who had not thought him seriously ill. I was invited to the autopsy, and observed, when the corpse was uncovered, a few dark-red spots on the surface, which were supposed to be petechial, the principal symptoms of his attack having been gastric, with great debility, as we were informed. The coffin was taken to a New England village for burial, where at the funeral some of the relatives approached and opened it to see the face of the deceased before it was inhumed. Of this number eight were attacked with smallpox, no other person in the neighborhood being assailed.”

The infection of smallpox may be conveyed in the following ways:

1. Through direct exposure to the patient, or to infected secretions and excretions.

2. Through contact with objects which have been infected by the patient—for example, sick-room articles.

3. Through infection carried in the clothing or on the person of healthy individuals.

4. Through air transmission.

5. Through transmission by insects and domestic animals.

Infection through Direct Exposure to the Patient.—The vast majority of cases of smallpox result from exposure to individuals suffering from

¹ *Vide Nouveau Dictionnaire*, article Contagion.

the disease. Smallpox is the most typical example of the contagious or catching disease. The briefest possible exposure on the part of a susceptible person will suffice to produce the disease. Many victims never discover the source of their infection; this is not so surprising when we appreciate the fact that the patient may impart the disease before the appearance of the eruption. That smallpox may be transmitted during the initial stage is undoubtedly proven by the records of cases in which the infection was received from individuals suffering from *variola sine exanthemate*. Persons are also frequently exposed to patients suffering from extremely mild and unrecognized forms of smallpox. The patients may not deem themselves ill and may after the initial illness continue their daily labors, in this manner unconsciously endangering the health of those with whom they come in contact. We recall, during the mild epidemic of smallpox of several years ago, a negro who drove a carriage along one of the principal thoroughfares of this city, who, though in the pustular stage of smallpox, did not feel sufficiently ill to remain at home. Time and time again have we been informed by patients that they came to the hospital in street cars. Some, too, admitted having travelled on the railroad from cities more or less distant while suffering from the disease in its early stages.

The fact is conclusively proven that the degree of severity of the attack produced in the second person bears no relationship to that in the infecting individual. We recall the case of a fatal hemorrhagic smallpox in a pregnant woman who received the infection from her father-in-law, whose attack was so mild as to escape unrecognized. There are on record reports of a few epidemics in which smallpox was uniformly mild, but ordinarily the severity of an attack of smallpox is measured by the susceptibility of the victim.

A robust constitution is no safeguard against variolous infection; in fact, some writers consider persons in good health more susceptible to the disease, on the same principle that ruddy children take vaccination more easily than weaklings.

Sometimes extensive epidemics arise from the importation into the community of a single patient suffering from the disease. One of the most remarkable instances of rapid diffusion of smallpox is the epidemic in Montreal in 1885, recorded by Osler. The city was visited by smallpox from 1870 to 1875, after which it died out, owing to vigorous vaccination and the exhaustion of suitable material. For ten years the city remained free of the disease. The French Canadians, being as a class opposed to vaccination, a large unvaccinated population grew up in this period. On February 28, 1885, a Pullman car-conductor, who had arrived from Chicago, where smallpox was prevalent, was removed to the Hôtel Dieu, the civic smallpox hospital being at that time closed. Isolation was not practised, and as a result a servant in the hospital contracted the disease and died. After this occurred, "with a negligence absolutely criminal, the hospital authorities dismissed all patients who presented no symptoms, who could go home." The disease spread like fire in dry grass, and within nine months 3164 persons died of smallpox

Infection through Sick-room Objects.—While the contagium of smallpox is perhaps more commonly conveyed from person to person through the atmosphere, this is by no means the only medium of infection. The infecting germs become attached to all objects in the immediate vicinity of the patient, and cling to them for a variable period of time. Objects which have a rough, shaggy surface, such as blankets, woollen clothing, etc., not only become more intensely infected, but hold the infection much longer than smooth objects. Woollen garments closely packed and excluded from the air as completely as possible have been known to retain the infection for many months or even years. If, however, such garments be freely exposed to the atmosphere and sunlight, the contagium will soon be destroyed. Of course it may be destroyed at once by disinfecting agents.

Buck¹ recounts the history of a case which illustrates the persistence of variolous infection. In 1876 a child was treated for an attack of smallpox in a New York house, after which the sick-room was thoroughly disinfected, the walls washed, and the carpets removed. Two years later (1878) an unvaccinated two months' old child of new tenants occupying the same room fell ill with smallpox, although it had never been out of the apartment. No smallpox was present in New York at the time.

Infected objects may convey the contagium over long distances, even over many hundreds of miles. In 1898 we saw a case of smallpox in this city in which we believe the infection was received from a bale of cotton brought from the South. Smallpox was prevalent in the cotton-growing districts of the Southern States, and was of such a mild type that the negro patients would frequently be in the fields gathering cotton while the eruption was developing or the scabs dropping off.

The case occurred in a man employed in a Philadelphia mill where cotton goods were manufactured, and which had received cotton from the South. At the time no cases of smallpox were present in Philadelphia or its vicinity, nor had there been for a period of two or three years. The man had not been out of the city for a long time. In seeking for the source of the infection we could arrive at no other conclusion than that it had been derived from a bale of cotton.

Infection Carried by Healthy Individuals.—Not only objects in the room, but also healthy persons whose duties require them to come in contact with the sick, may be the means of communicating the infection. The infection may adhere to the hair, the hands, and other parts of the body of the attendants, but the chief danger is from their clothing.

That healthy individuals may carry the infection has been conclusively demonstrated to us. We have, on a number of occasions, had brought into the hospital infants suffering from smallpox who had not been out of their homes, and who lived in neighborhoods free of the disease.

Great caution should be observed by physicians, nurses, and others in attendance upon smallpox patients. The exercise of proper care will

¹ *Treatise on Hygiene*, New York, 1879.

reduce the chances of carrying infection to a minimum. The writers have come in contact with thousands of smallpox patients, but by the exercise of great care have never to their knowledge conveyed the disease to a single individual.

Air Transmission of Smallpox Infection.—The contagium given off from a patient suffering from smallpox is of a volatile character, capable of surcharging the atmosphere of the sick-room. The older writers believed that the sphere of contagious influence of smallpox was extremely limited.

Haygarth, quoted by Gregory, was of the opinion that it did not extend "more than a few feet from the patient's body."

Hirsch says that the smallpox contagion "can be spread by atmospheric currents within a small range," and that there is "no mathematical expression to be found for the extent of that range; at the utmost it extends no farther than the immediate surroundings of the sick."

English physicians have within recent years devoted considerable study to the determination of the striking distance of the disease.

In the epidemic of 1881, Mr. W. H. Power,¹ after excluding all possible infection through ordinary intercourse, formulated an hypothesis of atmospheric convection of the smallpox poison. He assumed that smallpox infective material was "particulate," and that certain favorable conditions could disseminate such particulate matter over an area of a quarter or half a mile.

The particulate matter, or infectious dust, may be held in suspension in the water particles in the air, in fog and mist, and may be driven by air currents and deposited at some distance. During periods of stillness of the air about the hospital the infection is taken up and then wafted by the winds. The absence of ozone in the atmosphere is also said to be favorable to spread of infection. Periods of small movement of air and absence of ozone are said by Mr. Power to have preceded each of the more notable epidemic extensions in the neighborhood of the Fulham Hospital.

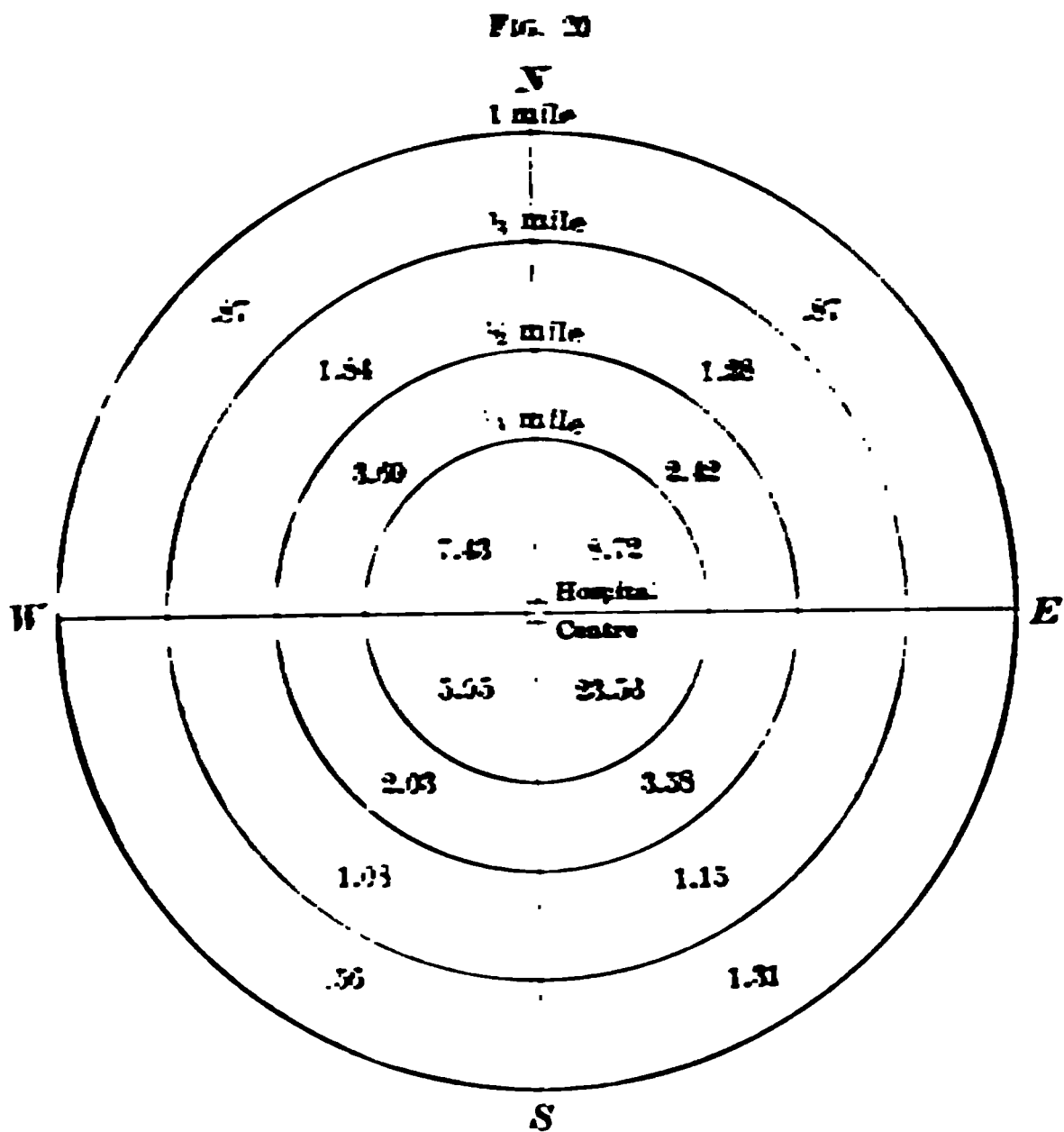
Parkes² says: "The exceptional incidence of smallpox in the immediate neighborhood of some of the London Smallpox Hospitals can admit of but one explanation, viz., that when a sufficient number of cases in the acute stages are collected together in one building on a small area of ground, the hospital becomes a centre of infection to the surrounding neighborhood." (See Fig. 20.)

"As regards the number of cases aggregated in a hospital necessary to enable it to exert an influence on the surrounding neighborhood, Dr. Power's reports of 1884-85 show that this influence was exerted when the number of acute cases had been restricted to twenty, while on one occasion he found the excess of smallpox in the neighborhood of the Fulham Hospital was quite remarkable at a time when the total admissions to the hospital had not exceeded nine, only five of these being cases in an acute stage."

¹ Supplement to Local Government Board, 1880-81, also 1884-85.

² Hygiene and Public Health, London, 1901.

Mr. A. W. Blyth¹ remarks: "The usual spread of smallpox is from person to person, but, from inquiries which have taken place as to the influence of smallpox hospitals upon a surrounding population, it is certain that the infection can strike at a distance.



Special area around Fulham Hospital divided into sections of $\frac{1}{4}$, $\frac{1}{2}$, $\frac{3}{4}$, and 1 mile radii, showing in the different areas the number of houses out of every 100 invaded by smallpox from May 25, 1884, to September 26, 1885.

Between N. and W. the hospital was greatly isolated from traffic because of few roadways.
Belt of houses between W. and S. comparatively narrow.
Between N. and E. houses few within $\frac{1}{4}$ mile: beyond they completely encompass the hospital.
The so-called special area was within 500 feet from the hospital centre.

The influence of the Sheffield Hospital in the epidemic of 1887-88 could be distinctly traced for a circle of four thousand feet: the following percentages of households attacked at successive distances from the hospital are given in the original reports by Dr. Barry,² inspector of the Local Government Board for England:

0 to 1000 feet	1.75	Percentage of houses attacked at varying distances from Sheffield Hospital.
1 " 2000 "	0.50	
2 " 3000 "	0.14	
3 " 4000 "	0.05	
Elsewhere	0.02	

The possibility of smallpox spreading by aerial infection increases greatly both the hospital difficulty and that of individual isolation."

¹ Manual of Public Health.
² Report of an Epidemic of Smallpox at Sheffield, 1887-88; London, 1889.

Evans,¹ from observation of a smallpox epidemic at Bradford, came to the same conclusion as Barry. During the year 1893, 626 domiciles were attacked by smallpox within a radius of a mile of the Bradford Fever Hospital.

There were 17,000 houses in the one-mile area about the hospital; of the 626 houses newly attacked, 162 were located within the quarter-mile limit, 242 between the quarter-mile and the half-mile boundaries, and 59 within the three-quarter-mile and one-mile limit. The rate of incidence of smallpox in 100 houses in the whole borough was 1.6; in the special one-mile area about the hospital, 3.6; and in the remainder of the borough, 0.6.

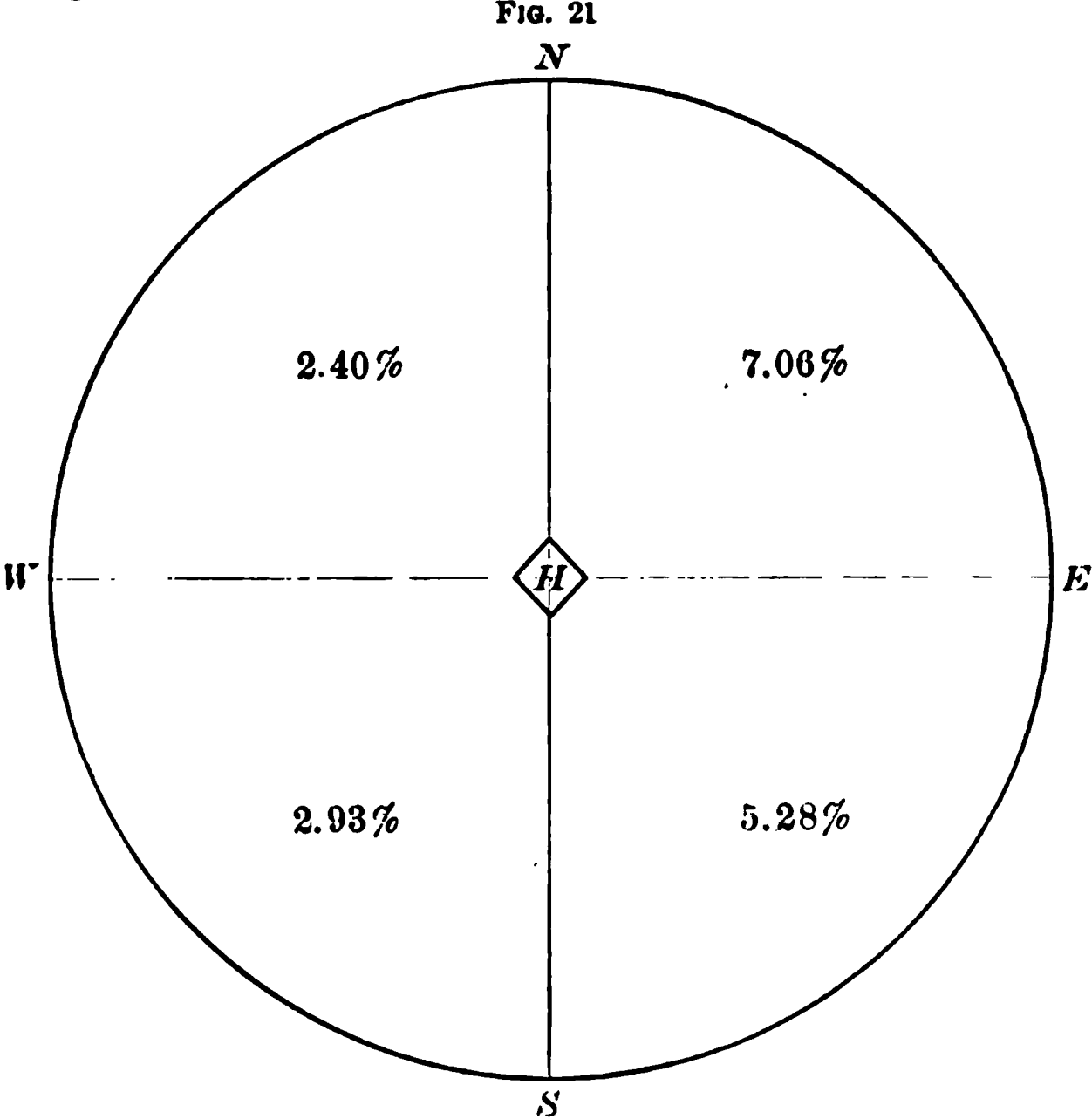


Diagram showing the influence of the wind in disseminating smallpox. (Evans.)

Within the quarter-mile circle about the hospital the rate was 10.4 per cent.; between the half-mile and the three-quarter-mile, 2.1 per cent. Evans believes that the extensive prevalence of smallpox within the special area about the hospital is to be explained on the grounds of aerial transmission of infected material from the wards of the hospital.

This view he believes is confirmed by a study of the direction of the prevailing winds during the year 1893.

Evans calculated the percentage of infected houses in the four quadrants of the circular mile area about the hospital as follows:

Northeast quadrant	7.06 per cent.
Southeast	"	5.28 "
Northwest	"	2.40 "
Southwest	"	2.93 "

¹ British Medical Journal, 1894, vol. ii. pp. 356-358. Quoted by Moore.

"These figures," he says, "are readily explained by the fact that on 250 days of the year the prevailing winds were westerly, and only on 83 days was the wind persistently from the east.

"During the first half of the year, when easterly winds were more common than during the second half, the proportion of cases occurring on the western side of the hospital was relatively greater than during the remainder of the year, when the easterly winds were less frequent."

Thresh,¹ from a study of smallpox outbreaks in the neighborhood of the smallpox hospital ships in the Thames River, says: "The extent of the area around a smallpox hospital which may be affected directly and indirectly by the hospital is apparently much larger than has heretofore been supposed. In the case of the ships lying off Purfleet the influence is probably being felt at a distance of fully three miles, and the presence of a belt of water half a mile in width is powerless to arrest the contagion.

"There can be no doubt that the danger increases with the increase of the number of acute cases in the hospital, the infectivity not being marked until a certain degree of concentration is reached, and with the proximity to the hospital. With a small hospital (say, constructed for from ten to twenty or thirty cases), my impression is that there is but little danger of the disease being spread therefrom; but the danger cannot be said to be non-existent.

"With hospitals having 100 beds or more the danger is naturally much greater, and when we come to hospitals of the size of those required to cope with an epidemic in a large city the peril may be great indeed."

He further says: "The hospital ships were placed opposite Purfleet in 1884, and since that time there has been an excessive prevalence of smallpox in the Orsett district, and especially in that portion lying nearest the ships. Prior to these floating hospitals being established near Purfleet, smallpox was little more prevalent in the Orsett district than in the remainder of the county, and only one-third to one-fourth as prevalent as in the metropolis.

"The change since then has been most marked: from the same basis the disease has been seven times more prevalent in Orsett than in the remainder of the county, and two and one-half times more prevalent than in London."

DISSENTING VIEWS AS TO THE ATMOSPHERIC TRANSMISSION OF SMALLPOX INFECTION.—Certain writers dissent from the view above expressed as to the aerial convection of smallpox.

Seaton² believes that no adequate evidence has been adduced to prove aerial convection for hospitals situated in sparsely settled districts.

He speaks of an instance which came under his observation in which a number of unvaccinated children living within a stone's throw of a smallpox hospital did not take the disease until a child sick with small-

¹ The Lancet, February 22 and 26, 1902.

British Medical Journal, January, 1896, p. 582.

pox was brought to the house, and the unvaccinated children thus directly exposed to the contagion. This was regarded as evidence that the contagion of smallpox does not extend to any considerable distance through the air.¹

Savill² holds "that fresh air, being itself one of the best natural germicides, is very unlikely to become a vehicle for the conveyance of microbes, and that on a *priori* grounds, therefore, we would not expect the germs of smallpox to be carried beyond the limit of an ordinary room."

He carefully investigated the epidemic of smallpox at Warrington in 1892-93, which he reported to the Royal Commission on Vaccination, and concluded that there was no need to assume a theory of aerial convection to explain the spread of the disease.

Wallace,³ in discussing this epidemic, comments on some of the observations presented in Savill's report. He points out that aerial convection would not explain the spread of the epidemic, for (1) the numbers of infected houses do not work out in perfect keeping with a theory of proportionate distances from the hospital as a centre, and (2) the largest proportion of infected houses is not to be found in the quadrant opposite the prevailing winds.

EXPERIENCE OF PHILADELPHIA DURING THE EPIDEMIC OF 1901 TO 1904.—During the years 1901, 1902, and 1903 there occurred in the city of Philadelphia 3989 cases of smallpox. Throughout the entire epidemic the Twenty-eighth Ward, in which the Municipal Hospital was located, furnished by far the largest number of smallpox patients. Next to this ward, in smallpox incidence, came those adjoining it. In the Twenty-eighth Ward there were 144 cases of smallpox per 10,000 of population. In the entire city, exclusive of this ward, the rate was 29 per 10,000 of population. The Twenty-eighth Ward and several of the neighboring wards, representing 26.71 per cent. of the population, contained 53.67 per cent. of the smallpox cases.

Although we were at first skeptical concerning the aerial transmission of variolous infection from a smallpox hospital, the preponderating incidence of smallpox in the Municipal Hospital district and adjoining wards throughout the entire epidemic has forced us to accept this mode of dissemination of the disease as established.

Transmission by Insects and Domestic Animals.—Researches within recent years have established the fact that insects may, in a number of diseases, directly convey infection to the human subject. The infective agent may undergo evolutionary development in the insect, the creature thus acting as an intermediate host, or it may be carried upon the wings and feet.

In the warmer months of the year the common house fly abounds in the wards of hospitals. This insect is essentially a scavenger, and is particularly attracted by foul-smelling pus. It is a common sight in the summer season to observe swarms of flies foraging upon the purulent material upon the faces and hands of smallpox patients, the wings and

¹ British Medical Journal, August 5, 1882.

² Ibid., 1897, p. 1680.

³ James Wallace, Smallpox, London, 1902.

feet of the insects being frequently bathed in the contents of ruptured pustules.

We have undertaken investigations to determine whether or not the flies swallow the purulent material. Repeated microscopic examinations of the intestines of flies caught in the vicinity of smallpox patients demonstrated the presence of an abundance of streptococci and staphylococci, which are the predominating organisms in the late variolous pustules. These germs did not appear to be digested, for they took the ordinary stains well. The intestines of flies caught about ordinary households, on the other hand, contained no germs of this character, and, indeed, often no germs at all. Inasmuch as the causal parasite of smallpox is resident within the pustules, it is reasonable to suppose that it also is swallowed by the fly.

It is obviously impossible to present proof that flies transmit the infection of smallpox; but that they are capable of doing so appears strongly probable. A fly carrying upon his feet or wings the *contagium vivum* of variola would, on alighting upon a susceptible individual, offer every opportunity for infection. It is also possible for the swallowed germs to be deposited in the form of excrement upon the face or hands of an unprotected person.

The ordinary house fly, or *Musca domestica*, is, owing to the conformation of the mouth parts, incapable of biting. A form of stable fly, the *Stomoxys calcitrans*, frequently found in houses, does, however, pierce the skin. Such a fly might readily carry the infection of smallpox into the skin in the act of biting, and thus give rise to an inoculation form of smallpox.

To what extent flies and other insects contribute toward the spread of smallpox cannot be determined. As flies are capable of travelling a considerable distance, some cases of smallpox of mysterious origin might be explained through their agency.

That the transmission of smallpox through the medium of flies, however, is not an important factor in epidemics is evidenced by the fact that the disease spreads most in the cold months, when flies are absent, and least in the hot months, when they are abundant.

It is quite conceivable that dogs, cats, and other domestic animals occupying domiciles in which smallpox exists may carry the contagion of the disease in their fur. The closer the contact of such animals with the variolous patient, the greater is the likelihood of particulate infection being transferred. The roving of these animals might play some role in the dissemination of the disease within limited areas.

THE SYMPTOMATOLOGY OF SMALLPOX.

Period of Incubation.—From the moment that the microparasite of smallpox is received into the system certain subtle and unknown processes begin which, in the course of a more or less constant period of time, culminate in active clinical manifestations. To this latent breeding stage the term “period of incubation” is applied. The time

elapsing between the reception of the variolous poison and the outbreak of the disease can occasionally be determined with a considerable degree of accuracy. This is more easily accomplished in sporadic cases, where an individual has been exposed but once and for a brief period of time. Where the exposure is frequent or extends over a long period it is difficult to divine the exact moment when the infection is received. When the disease prevails in epidemic form it is not impossible for an unknown exposure to precede the one of which the individual has knowledge; in such cases the computed period of incubation would appear to be unusually short. Erroneous calculations of the duration of the period of incubation have doubtless arisen from failure to recognize this fact.

In the majority of cases in which we have had the opportunity of carefully studying the incubation stage, we have found it to be ten to twelve days, and we would, with other writers, regard this as the normal period. In a few instances it is true we have known persons to fall ill with smallpox after the raising of a two weeks' quarantine of the houses in which they were confined and in which smallpox had existed. We have also been able in a few cases to reckon with tolerable certainty a period of incubation of sixteen days, the eruption appearing on the eighteenth. Some writers have recorded instances in which the incubation period has been prolonged to twenty days. On the other hand, we have known a young physician, exposed to smallpox, to develop the first symptoms at the end of five and a half days, and the eruption at the termination of ten and one-half days. Ordinarily, however, the period is seldom less than eight days or more than fourteen.

The incubation period is ordinarily not characterized by any active symptoms. Patients usually pursue their daily occupations ignorant of the fact that there is developing within them a dread disease. There are, however, frequent exceptions to this rule. It is not rare for patients to lose their appetite and complain of lassitude, chilliness, headache, gastric uneasiness, etc. These symptoms, when they occur, are commonly noted during the last few days of the incubation period. They may, however, develop as early as a week before the invasive chill. Now and then a patient will complain of slight sore throat during the last days of this stage.

The Stage of Invasion, or Initial Stage.—This stage is frequently ushered in with suddenness and with considerable violence. The earliest symptom is most frequently a *chill*. This may be severe enough to be accompanied by chattering of the teeth, or it may consist of a succession of creepy sensations scarcely sufficient to attract the patient's attention. Synchronously with the chill or immediately following it the *fever* appears. The temperature on the first day often rises to 103° or 104° F., and on the second and third day, with perhaps the exception of slight morning remissions, it rises still higher, frequently reaching 105°, and in some cases even 107° F. The elevation of temperature is usually sudden; in but few diseases does it rise so quickly from the normal to a high degree. Even in varioloid the early symp-

toms are not infrequently equally severe, although occasionally they are so mild as to escape attention. But the eruption of unmodified smallpox seldom if ever appears without being preceded by a well-marked invasive stage.

During the continuance of the fever the skin is hot and sometimes dry. Profuse sweating, however, is by no means uncommon; this is apt to come on in the evening.

The *pulse*, as a rule, is full, tense, and rapid, its frequency generally corresponding with the temperature curve. In adults it varies between 100 and 130, while in children it not infrequently reaches 160. In some cases the pulse during the initial stage will be found to be relatively slow and entirely disproportionate to the height of the fever. We have on a number of occasions noted a pulse of 90, 80, and even 70, with a temperature of 104° or 105° F. These cases were seen in the hospital on the first and second day of the eruption; consequently we are not able to state whether this pulse rate was present at the onset of the initial symptoms.

The respirations are almost always increased in frequency, especially when the temperature is excessively high. Prostration is often extreme, being out of all proportion to the length of the illness. Strong and robust patients are frequently unable to stand without support, and when in the upright position soon become pale and liable to be attacked by vertigo or syncope. Thirst is great, the lips and tongue are parched and dry, and there is complete loss of appetite.

Constipation is a common symptom and is apt to persist throughout the course of the disease. The tongue is usually coated with a thick, yellowish covering, and the breath is heavy and offensive. According to some authors, the odor from the body of a patient at this stage of the disease is so peculiar and distinctive as to make it possible for the diagnosis of smallpox to be made by this symptom alone. We must confess that our olfactories have not acquired the degree of acuteness to detect such an odor.

Irritability of the stomach is a very frequent manifestation. Occasionally the first symptom noted by the patient is severe and persistent vomiting. In such cases the disease has on more than one occasion been regarded as gastritis. The *vomiting* often continues for two or three days. It is apt to be accompanied by marked tenderness and pain in the pit of the stomach. The irritability usually ceases when the eruption appears. When it continues longer it should be viewed with some solicitude. Especially in hemorrhagic smallpox is this symptom, together with epigastric pain, apt to be distressing and prominent. Nausea and retching are present in some cases without actual emesis.

Headache is the most prominent among the early nervous symptoms. It usually follows shortly after the chill, but in a certain proportion of cases it precedes it, being not infrequently the earliest evidence of illness. Its intensity varies greatly, corresponding in a measure with the height of the febrile action. At times it is so excruciating as to cause even self-restrained individuals to cry aloud. The face is often flushed,

PLATE VII.



Serial Photographs of Smallpox in an Unvaccinated Man.
Third Day of Eruption.

PLATE VIII.



Fourth Day of Eruption

PLATE IX.



Sixth Day of Eruption.

PLATE X.



Eighth Day of Eruption.

PLATE XI.



Tenth Day of Eruption.

PLATE XII.



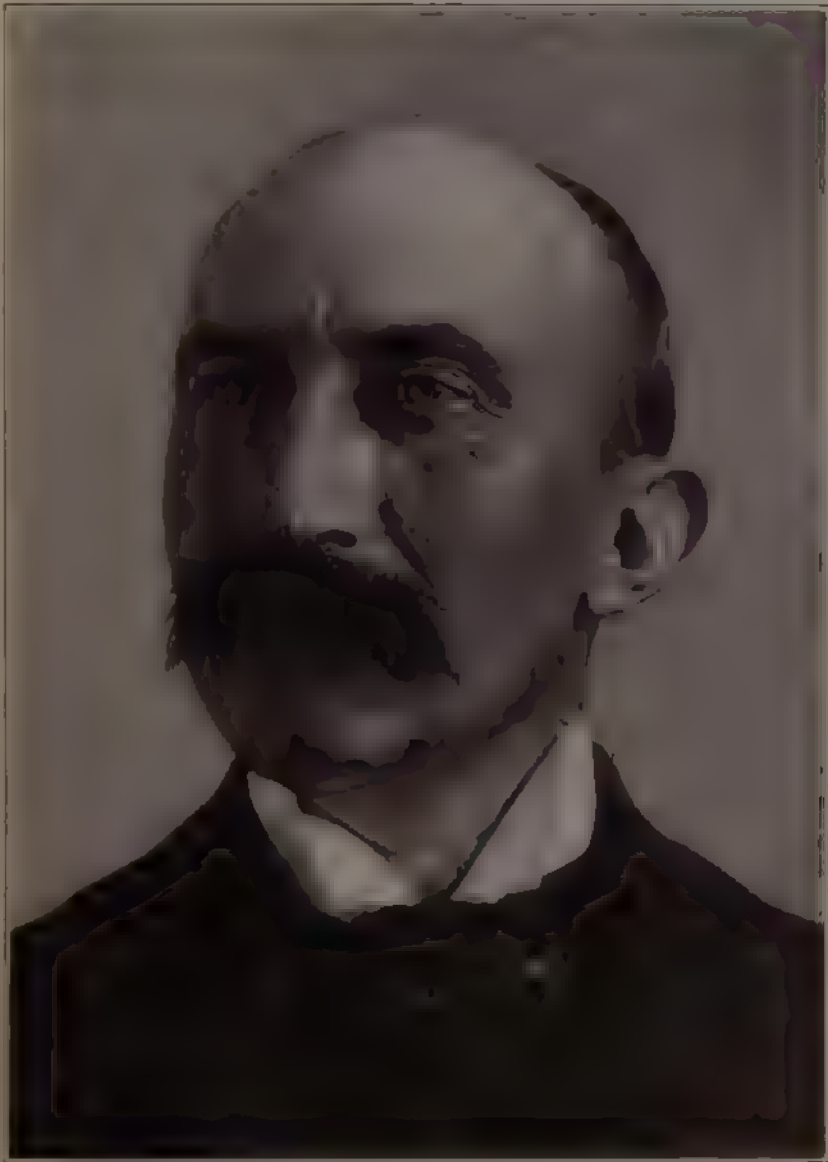
Twelfth Day of Eruption.

PLATE XIII.



Sixteenth Day of Eruption.

PLATE XIV.



After Recovery. Scarring present, but not deep.

the carotids visibly pulsating. Restlessness and sleeplessness are common symptoms during this stage. Children, on the contrary, are sometimes drowsy and sleepy. When the temperature is high, delirium is prone to supervene. This usually takes the form of talkative incoherence, although some patients become quite violent. Coma is rare in adults, but not uncommon in children. Convulsions are frequently seen in children, more so perhaps in this disease than in any other of the exanthemata. They may be severe and repeated, and may continue even after the appearance of the eruption.

Pain in the back is a symptom so commonly observed that it is believed to be of special diagnostic value. It is not as constant as some of the other symptoms, yet it occurs in more than one-half of the cases. In perhaps one-third of the cases it is sufficiently severe to cause the patient to volunteer information concerning it. Its diagnostic import, therefore, is due rather to its infrequency in the other acute infectious diseases than to its constancy in smallpox. The lumbar and sacral regions are the parts to which the pain is usually referred, although it may extend to the dorsal region. As a rule, it is more severe in unmodified smallpox than in varioloid, yet this rule is subject to many exceptions. In hemorrhagic cases the pain is often of an excruciating violence. Lumbar pain is more constantly seen among female than male patients, owing to the fact that the menstrual function is very liable to be excited by the initial illness of smallpox. In the vast majority of women who are stricken with smallpox the menses appear out of their regular period. This is true of mild as well as severe cases. The premature onset of the menstrual flow occurs with more striking frequency in this disease than in any other of the infectious maladies. Pregnant women are exceedingly liable to suffer from abortion or premature delivery. The pain in the back owing to these causes is given greater prominence in women.

General aches and pains are frequently complained of, appearing at the same time as the headache and backache. These may occur anywhere, but are usually referred to the lower extremities, particularly about the knees. The soreness of the general muscular system may lead to confusion of diagnosis with *la grippe*. *Vertigo*, which is particularly manifest upon the patients assuming the erect position, is a common early symptom. It is often well marked, even in mild cases, for these patients are more apt to rise from their beds. Syncopal attacks may occur in weak individuals.

Trousseau records having seen during the initial stage patients who suffered from temporary loss of power in the lower extremities, associated in a few instances with retention of urine. When this condition occurs, it is, in our experience, most likely to be encountered at a later period of the disease.

There is a considerable degree of variation in the character and sequence of the symptoms constituting the initial stage of smallpox. This is shown in the following analysis of 100 cases occurring in the epidemic of 1901 and 1902: The patients, who were taken without selection, were closely interrogated as to the nature and chrono-

logical development of the various symptoms. The number includes 28 cases of confluent smallpox, 15 with very profuse and semiconfluent eruptions, 29 with eruptions of moderate severity, and 29 cases of mild varioloid. Of this series of 100 patients, 22 died. Headache was the most constant of the initial symptoms. The various symptoms mentioned were present in the following percentages: Headache, 86 per cent.; chills or chilliness, 78 per cent.; backache, 70 per cent.; vertigo, 57 per cent.; vomiting, 55 per cent.; nausea without emesis, 10 per cent.

In some of these cases the symptoms were of marked severity, while in others they were extremely mild. An effort was made to determine the earliest symptom observed by these patients. It is recognized that some inaccuracy must arise from an attempt to chronologically arrange the symptoms from histories thus obtained.

Chilliness or a decided chill was the first symptom in	35 cases.
Headache was the first symptom in	26 "
Backache " " " "	16 "
Vomiting " " " "	9 "
General aches and pains were the first symptoms in	7 "
Vertigo was the first symptom in	2 "

In but 2 patients out of the 100 was there complete absence of initial illness; 1 of these was a man, aged twenty-six years, with a very mild varioloid, and the other a colored woman, aged twenty-seven years, with an eruption of moderate severity. Upon close inquiry the latter patient admitted experiencing fatigue upon the day preceding the eruption. It is possible that some negative histories of this character may be due to poor memory or lack of intelligence on the part of the patients.

In the severe cases the initial illness was always well marked, although the classic symptoms were not invariably present. A man, aged fifty-five years, who had a fatal confluent attack had merely as prodromes a severe chill, fever, and prostration; headache, backache, vertigo, and vomiting were absent. A male patient, aged twenty-nine years, with an eruption of moderate severity, experienced, during the initial stage, fever, repeated vomiting, and pain in the stomach, without any other symptoms. On the other hand, quite a number of patients with very mild eruptions gave a perfect history of the classic initial syndrome. A young woman of twenty years, for instance, with only three or four lesions on the face and a few upon the arms and hands, experienced, at the onset of the disease, headache, backache, repeated vomiting, severe chills, vertigo, and aching in the legs.

These observations are in accord with those of most writers, and seem to illustrate the impossibility of forecasting the extent of the eruption from the degree of severity of the initial symptoms. We have frequently seen the most aggravated febrile symptoms followed by a perfectly insignificant eruption. Mild initial manifestations are rarely succeeded by a severe cutaneous outbreak. In general terms it may be stated that severe initial symptoms may be followed either by a profuse or a sparse eruption, and that mild initial symptoms are nearly always followed by a mild eruption.

The *urine*, in the initial stage, is usually more or less diminished according to the degree of the fever. The solid constituents are not out of their normal proportion, except the chlorides, which are considerably diminished. In severe cases, especially those about to become hemorrhagic, albuminuria may be present. A high grade of fever might be responsible for a small quantity of albumin, but if it be present in great abundance a malignant type of the disease should be suspected. Before giving an unfavorable prognosis, however, care should be taken to exclude the possibility of pre-existing disease of the kidneys.

The *spleen* may be found enlarged in the initial stage of severe smallpox. In mild cases no enlargement, as a rule, can be detected.

Peculiar *prodromal rashes* often make their appearance during the initial illness. When they develop it is usually upon the second day of the invasive fever. They disappear ordinarily in from twenty-four to forty-eight hours. They may, however, continue several days after the appearance of the eruption. The frequency of these rashes appears to vary in different epidemics. During the widespread and malignant epidemics of 1871 and 1872 they were very common. Osler noted these rashes during this period in 13 per cent. of his cases. These eruptions are not so apt to be observed in smallpox hospitals, inasmuch as they disappear commonly before the diagnosis is made and the patient conveyed to the hospital. The most common type is that *resembling measles*, with which disease, indeed, it is liable to be confounded. The eruption has an irregular distribution, being at times generalized and at other times limited to certain regions of the body. It, moreover, differs from the eruption of measles in that the rash is not elevated above the level of the skin and therefore scarcely appreciable to the finger when passed over it. Its ephemeral character is also a differentiating feature. This *roseola variolosa*, as it has been designated, has a close analogue in the *roseola vaccinosa* which occasionally appears about the ninth to the eleventh day after vaccination.

The *scarlatiniform* rash is less common than the measles-like eruption. It may involve a large part of the cutaneous surface, but is more apt to affect certain areas, as the thighs, inguinal regions, extensor surfaces of the extremities, and the trunk. Some authors refer to the appearance of an urticarial eruption in rare cases.

The *petechial* or *hemorrhagic* initial rash has a special predilection for certain regions of the body which were carefully studied by Simon, of Hamburg. This writer pointed out the frequent occurrence of the eruption in the lower abdominal, inguinal, and genital regions and inner aspects of the thighs, constituting a triangle whose base traverses the neighborhood of the umbilicus (the so-called crural triangle of Simon). The "axillary triangle," including the inner aspect of the arm, axilla, and pectoral region is also a commonly affected area. The petechial rash is also frequently seen along the lateral surface of the thorax and abdomen. The eruption consists of closely aggregated, pinpoint to pinhead sized, purplish or clarety spots, which are in such intimate juxtaposition as to convey the impression of a diffuse redness.

Being the result of a hemorrhagic extravasation into the skin, the discoloration does not disappear upon pressure.

Occasionally an erythematopetechial rash is seen, the eruption partaking of the characters of both the erythematous and hemorrhagic rashes.

The petechial eruptions may occur in cases which later prove to be quite mild. More often, however, they are the harbingers of severe smallpox of the hemorrhagic type. The morbilliform eruptions in our experience are much more common in cases of varioloid, and their occurrence, therefore, may be regarded as an auspicious sign. We are able to recall two cases of smallpox in vaccinated individuals in which the roseolous eruption was practically the only cutaneous manifestation. In one of these cases, it is true, about half a dozen small variolous papules appeared as the initial rash faded away, but they disappeared in two or three days without becoming in the slightest degree vesicular. These cases belong to the class commonly designated *variola sine exanthemate*, which is the most benignant form that smallpox may assume. That such cases are occasionally encountered is evident from the writings of both ancient and modern authors. Perhaps in every epidemic patients are seen who give a history of exposure to smallpox and who, in due course of time, are suddenly seized with chills, followed by headache, fever, vomiting, prostration, and pain in the back. These symptoms continue for three or four days, and then subside without the development of any eruption except perhaps one of the prodromal rashes to which reference has been made. It is impossible to explain such cases on any other supposition than that the disease was *variola* without the eruption. Trousseau refers to cases observed by him in which the only symptoms characteristic of the disease were a "few pustules on the pharynx and the pendulous veil of the palate."

It may be of interest to record the histories of two patients under our observation upon whom but a single variolous lesion appeared:

B. H., aged twenty-six years, suffering from measles, was sent into the Municipal Hospital under the erroneous diagnosis of smallpox. He was immediately vaccinated, but this and subsequent attempts failed. At the end of ten days he was seized with high fever (104° F.), headache, and vomiting. A few days later a single papule appeared in the right loin. This went on to vesicle formation, becoming characteristically umbilicated, but dried up within a few days. The patient claimed to have had smallpox at the age of eight years, but showed merely a single pit upon the face.

The following case presents a somewhat similar history:

W. G., a colored lad, aged fifteen years, was vaccinated four years prior to admission; he presents a good vaccination cicatrix. He was brought into the hospital from a house from which several patients with smallpox were removed. On admission he had a temperature of 102° F. and presented other well-marked initial symptoms. On the subsidence of these symptoms he developed a single typical papule on the trunk.

These cases come almost within the definition of variola without an exanthem. If smallpox may occur with the appearance of but one lesion, there is no reason why it should not at times develop without any eruption whatsoever.

The duration of the initial stage is commonly forty-eight to seventy-two hours; it is rarely less, but it may be somewhat prolonged. Trousseau held that the longer the eruption was delayed in its appearance, the more favorable was the prognosis. This is scarcely borne out by experience. It is misleading to draw any prognostic conclusions from the duration of this stage.

It is commonly stated in text-books that upon the appearance of the eruption of smallpox the fever subsides and a general abatement of the systemic symptoms occurs. In our experience a decided remission in the temperature does not take place in unmodified smallpox until the second, third, or fourth day of the eruption. In very mild cases, more particularly in those modified by previous vaccination, the temperature may fall to normal as the exanthem makes its appearance. With the fall of the fever there is a cessation of the pains and a general improvement in the condition of the patient. In mild cases of varioloid the illness of the patient is terminated at this stage. In severe cases the improvement constitutes but a brief respite, and then the grim struggle with the disease begins.

Stage of Eruption.—By carefully observing the early stage of the disease it will be found that the true eruption makes its appearance with remarkable regularity on the third day of the illness, calculating from the day on which the initial chill or rigor occurred. In modified smallpox deviations from this rule may be noted. The eruption almost always appears first on the forehead and temples near the edge of the hair, and on the wrists. Not infrequently it is seen first on the upper lip and around the mouth. It rapidly spreads to the scalp, face, neck, ears, forearms, and hands, always showing a decided preference for the cutaneous surfaces habitually exposed to the atmosphere. In the course of twenty-four hours, sometimes somewhat earlier, it extends to the body and lower extremities. It does not simultaneously affect these regions, but attacks in succession the back, arms, breast, and finally the legs and feet. In rare cases the exanthem may be first noted on the trunk or extremities.

The full complement of lesions does not make its appearance at once in any given part; the eruption continues rather to multiply for two or three days before its definite limit is reached. In varioloid new lesions may continue to appear for a longer period of time. Upon carefully examining the eruption it is seen that many lesions develop at the sites of hair follicles or orifices of the sebaceous and sudorific glands.

The eruption begins as small red spots or *macules* some of which may be so small and faint as to be scarcely visible, while others reach the size of a lentil-seed. The color is at first pinkish-red, later assuming a deeper tint. In many cases the lesions on the trunk and extremities present the appearance of flea-bites. The lesions gradually increase in

size and number, becoming more and more prominent, so that in twenty-four hours they assume the form of elevated *papules*, with a characteristic feel. The early papules, particularly about the forehead and cheeks, may be more demonstrable to the sense of touch than to the eye. They possess a peculiar induration, and convey to the finger a sensation similar to that which would be produced by grains of shot embedded in the skin. The "shotty" feel varies in degree in different cases. Some papules are extremely hard, while others possess comparatively little induration. They are at first always discrete, but they may rapidly increase in number and become confluent, even before the vesicular stage is reached.

On the third day of the eruption, or the fifth day of the disease, very many of the lesions which made their appearance first will be found to contain a little clear serum. Indeed, in many patients, one will be able to note on the second day a lesion here and there which has become vesicular in advance of the general eruption. These precocious vesicles are frequently of diagnostic import, enabling one in doubtful cases to assert the variolous nature of the disease. By the fourth or fifth day all of the lesions are converted into *vesicles*. At this stage they commonly have the size and shape of a split-pea. Small vesicles are apt to be conical or acuminate, while the larger lesions have a convexly flat or hemispherical appearance. The vesicle of smallpox is extremely firm; not infrequently it feels harder to the finger than the papule from which it developed. In no other disease do the vesicles acquire such a degree of induration and hardness. The color of the vesicle is at first pinkish, the tint extending to the areola surrounding it. Later, as the fluid exudation into it increases, it assumes a peculiar opaline or pearly hue. This, with the shining and glistening surface, imparts to the vesicle a most distinctive appearance. One of the most characteristic features of the smallpox vesicle is the so-called "umbilication." In the smaller acuminate vesicles this is seen as a minute central depression or invagination, representing in all probability the mouth of a hair follicle or sweat duct. This form of umbilication may occasionally be met with in other cutaneous diseases, when the lesions are situated at the mouths of the pilary or sudoriparous orifices. In the larger, pea-sized vesicles the umbilication is seen as a round, oval, or slightly irregular indentation. In this case the depression is flatter and is probably due to the bulging of the periphery of the pock. This latter form of umbilication is of important diagnostic value, as but few other vesicular diseases produce quite the same appearance. The forearms and the backs of the hands are, perhaps, the regions upon which umbilication is most characteristically seen. Umbilication is only observed in a certain proportion of vesicles. It is by no means a constant feature of smallpox eruption and, indeed, is not infrequently absent altogether. This is particularly true of cases of varioloid. A form of secondary umbilication is commonly seen during the stage of decline or desiccation, when the pustules, as the result of rupture or drying, show a depression in the centre.

If one observes closely the large, clear vesicles of about the fifth or sixth day, particularly those situated on the dorsal surfaces of the hands, one can frequently discern through the epidermal roof something of the interior construction of the lesions. They will be seen to be made up of compartments which are divided by vertical septa, very much like the divisions of an orange. The vertical partitions are formed by the spinning out and reticulation of the epithelial cells of the rete mucosum. This accounts for the multilocular character of the smallpox vesicle, and explains the inability to completely evacuate its contents by a single puncture. Large, fully developed vesicles frequently show at their central summit a disk of the color of yellowish serum, and around the periphery a whitish, puriform ring looking not unlike an *arcus senilis*.

The predominance of the eruption of smallpox on the face and terminal extremities is to be accounted for by the greater vascularity of the skin in these regions. That lesions are attracted by an overfilling of

FIG. 22



Smallpox eruption showing confluence over an area upon which iodine had been applied before the eruption appeared

the cutaneous vessels is seen in the excessive development of the eruption wherever the skin has been irritated or congested. It is a common experience in the hospital to see in a discrete case of smallpox a profusion of lesions over a rectangular area in the lumbar or epigastric region where a mustard plaster had been applied during the initial stage for the relief of pain. Fig. 22 shows a marked confluence of the pustules in the form of a band on the wrist where the patient had applied iodine for a sprain received before his illness. An intense coalescence of the eruption upon the forearm is seen in Fig. 23. This was occasioned by the presence of a sunburn upon these parts.

It is only when mechanical or chemical irritation is applied to the skin before the appearance of the eruption that an increase in the number of lesions is produced. We have frequently applied tincture of iodine and similar applications to the skin in the early days of the eruption without augmenting the variolous crop in the region thus treated. Some of the older physicians purposely irritated the skin of certain

portions of the body with the hope of deflecting the eruption from the face to the regions thus treated. Unfortunately, the eruption was increased in the manipulated areas without diminishing the number of lesions on the face.

FIG. 23



Smallpox eruption showing areas of extreme confluent which had been the seat of a sunburn, before the eruption appeared.

Stage of Suppuration.—The contents of the vesicles gradually become more and more turbid, as the result of the increased exudation of leukocytes, until the lesions become frankly purulent. This condition is usually reached in unmodified smallpox about the sixth day of the eruption, and marks the beginning of the stage of suppuration. The pustules now, in good part, become large and globular, and stand out prominently from the skin. Their color varies somewhat in different cases. At times the pustules acquire a distinctly yellowish tint not unlike the color of ordinary pus. Frequently, they retain until ruptured a peculiar chalky or grayish-white hue. The reddish areola, which is observed about the vesicles, develops in this stage into a broader, deeper-hued, violaceous halo. Where the lesions are closely aggregated the entire interpustular integument becomes reddened and tumefied.

PLATE XV.



Well-pronounced Discrete Smallpox in an Unvaccinated Subject on the Eighth Day of Eruption, showing the relative sparsity of the lesions upon the trunk.

On the face and scalp, where the eruption is apt to be profuse, the redness and intumescence are so extreme as to render the features of the patients completely unrecognizable. The eyelids, as the result of oedema of the loose areolar tissue, become enormously puffed and completely close the palpebral cleft, which is bathed in a puriform secretion. The patient for a time is unable to see, owing to a complete closure of the eyelids. The lips, nose, and ears are distorted, the normal contour of the face is lost, and the entire head swollen beyond human proportions. The patient presents a most revolting and loathsome appearance. One seeing the disease for the first time in this stage is apt to be appalled by the horrible spectacle. The patient is sorely distressed by the inflammation and swelling of the scalp, inasmuch as contact with the pillow is a source of unendurable pain.

FIG. 24



Discrete smallpox eruption on the ninth day, showing marked oedema of the face, completely closing the eyelids.

As the eruption on the body and lower extremities is later in making its appearance than that on the face, so also is it later in reaching maturation. When the lesions upon the face have become vesicular, it will be found that the efflorescence upon the trunk and extremities is still in the papular stage. In like manner the facial lesions will have advanced to pustulation by the time that the eruption on the body has become vesicular. There is noticeable, therefore, this regular multiformity in the character of the lesions upon the different portions of the body. About the eighth day the pustules on the face have reached their greatest development, and the process of retrogression then begins. They become yellowish, present a shrunk or shrivelled appearance, and rupture or collapse. On rupturing the pustules give exit to a viscid, glairy, dirty-yellow pus, which dries in the form of yellowish or brownish crusts. A gradual subsidence in the inflammation and swelling takes place, and the normal outlines of the face are once more restored.

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FIG. 24



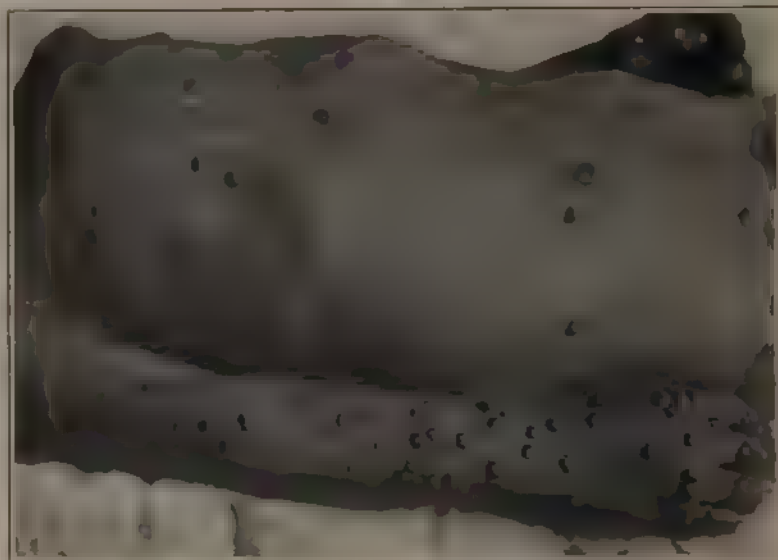
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During the stage of pustulation the lesions which exhibited umbilication become distended and globular, thus effacing the central depression. The epithelial bands holding down the centre of the lesion, in all probability become dissolved away, permitting the roof of the pustule to assume an hemispherical form.

The eruption on the trunk is almost always much less abundant than on other parts of the body. Not infrequently the hypogastrium is quite free from pustules, even when the face and hands show a marked degree of confluence. Exceptions to this rule are, however, occasionally met with. We have seen patients the skin of whose body was so profusely covered that it would have been impossible to place the tip of the finger

FIG. 25



Large tall pustules on the seventh day of the eruption.

upon a healthy area of skin. Of course, in such cases the danger to the patient is correspondingly increased, inasmuch as the gravity of the disease is, as a rule, directly proportionate to the extent of the eruption.

In a well-pronounced case of semiconfluent smallpox under our care an approximate count of the number of lesions was made. This was accomplished by dividing the cutaneous surface into certain areas by means of a colored crayon and counting the pustules within these boundaries. Upon the face and scalp the confluence of the pustules precluded the possibility of their being counted. A conservative estimate of the number present was therefore made.

The number of lesions computed upon the different portions of the body is herewith appended:

PLATE XVI.



Smallpox in an Unvaccinated Negro on the Eighth Day of Eruption. Confluent on face, semiconfluent on extremities, and discrete on trunk.

PLATE XVII.



Moderately Severe Form of Smallpox in an Unvaccinated Negro on the Eighth Day of Eruption. Semiconfluent on face, discrete on trunk, and extremities.

Total on fingers of one hand	Thumb	61	}	. . .	392
	Index finger	97			
	Middle "	95			
	Ring "	81			
	Little "	58			
Dorsal surface of one hand	382
Palmar " " "	129
Total lesions on both hands	1,806
Forearms	4,400
Arms	2,840
Chest	1,000
Abdomen	175
Thighs	4,180
Legs	2,850
Feet	750
Back	5,700
Estimated number on face and scalp	3,000
Total	26,701

By evacuating some of the pustules with a pipette we estimated that the lesions at the height of their development each contained about three drops of pus. Such a computation developed the surprising fact that the patient referred to carried in his skin about five quarts of pus.

We have seen large men with more profuse eruptions, who must have had in the neighborhood of forty thousand pustules. With this prodigious amount of purulent material in the skin the wonder is that any patient thus afflicted should recover.

The pustules on the trunk appear to have a more superficial seat in the skin than on cutaneous surfaces constantly exposed to the air; hence they are not accompanied by the same amount of inflammatory swelling or ulcerative destruction of the cutis. There is, moreover, very little tendency on the trunk and lower extremities to confluence of the lesions. We frequently note a coalescence of two or three pustules as a result of their contiguity, but the vast majority of the lesions remain discrete.

This statement, however, does not apply to the efflorescence *on the hands and feet*. In these regions the degree of confluence may be intense and cause the patient great suffering. As a result of the thickness of the overlying epidermis on the palms and soles, the pustules do not acquire as great a prominence as elsewhere. Being bound down by the tense and unyielding horny layer of skin, pressure is made upon the delicate underlying cutaneous nerves, producing distressing pain. In a severe attack of smallpox the palms and soles, the fingers and toes, and the dorsal surfaces of the hands and feet are profusely covered. When the pustular stage is reached the patient becomes perfectly helpless; he is unable to feed himself or in any way utilize his hands. It is pitiful to behold him in bed, with his hands and fingers semiflexed, and his arms outstretched for fear of the dreaded contact with the bed-clothing. At times the pustules on the back of the hands fuse and produce large bullæ, or even an extensive undermining of the epidermis similar to that seen in a bad scald.

During the suppurative stage a most penetrating and offensive odor

emanates from the body of the patient, and from the pus-stained bed and body linen. This stench results from the decomposition of the effete and purulent discharge, and is not peculiar to smallpox. In neglected cases the odor is most sickening, and may pervade the atmosphere of a room or, indeed, of an entire house.

Eruption upon the Mucous Membranes.—Simultaneous with the appearance of the smallpox efflorescence upon the cutaneous surface, or a little earlier, the eruption develops upon the adjacent mucous membranes. The involvement is almost exclusively confined to those mucous surfaces which are near the external orifices, or to which the air has access. The eruption early attacks the lining of the

FIG. 25



Well-pronounced smallpox on the eighth day, occurring during a particularly mild epidemic, the lesions being very superficial.

mouth, nose, and pharynx, and in severe cases the larynx, bronchi, and œsophagus. The extent of the enanthem bears a direct relation to the severity of the eruption of the skin. The lesions, however, are seldom as profuse upon the mucous surfaces as upon the integument. If an examination of the mouth and fauces be made at the very beginning of the eruptive stage, small yet distinct red spots may be seen upon the roof of the mouth, buccal surfaces, and anterior arches of the palate.

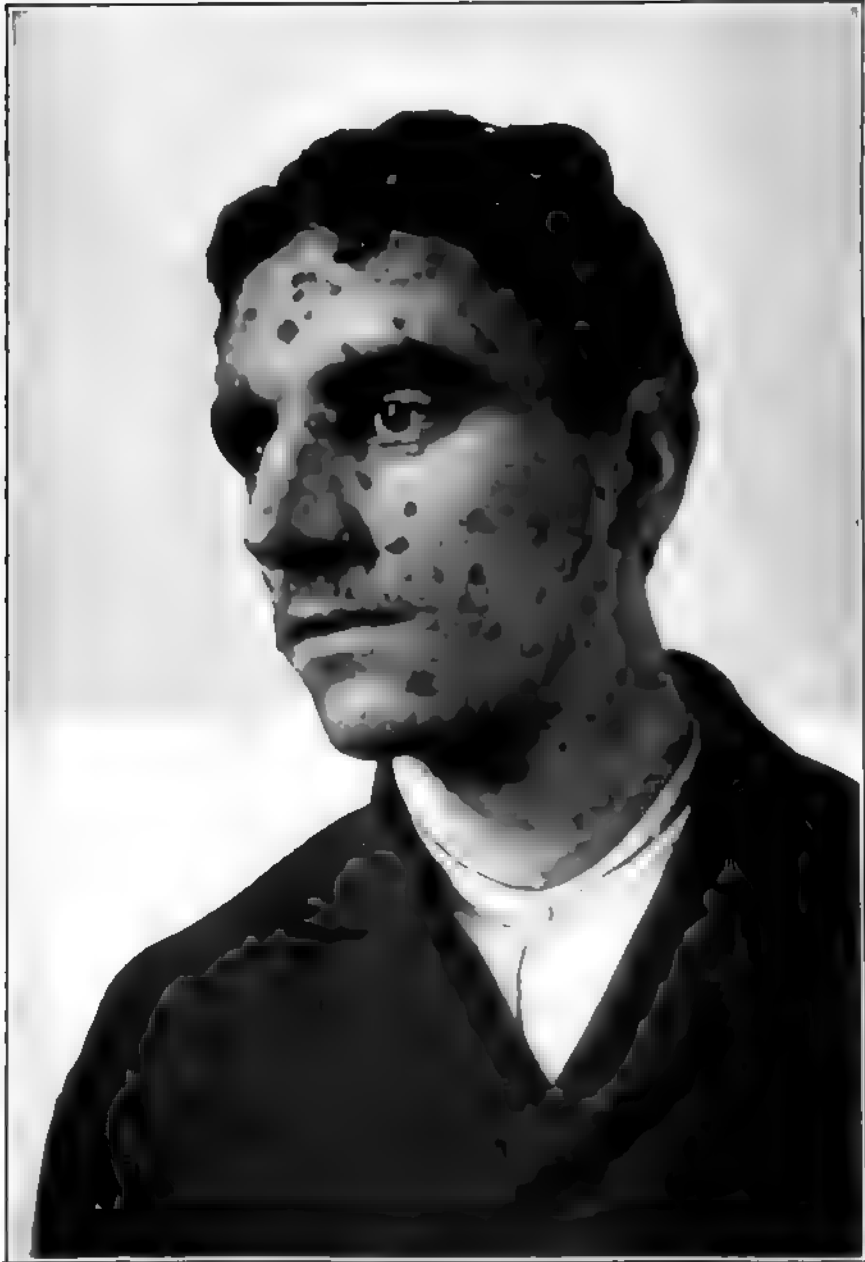
These macules are pinhead sized and larger, and of an intense red color, which contrasts with the violaceous or bluish-red tint of the surrounding mucous membrane. In a short time the spots become slightly elevated or papular, frequently exhibiting a whitish, glistening centre. The parallelism with the evolution of the cutaneous pock ceases at this

PLATE XVIII.



Mild Discrete Variety of Smallpox. Seventh day of eruption.

PLATE XIX.



Discrete Smallpox, with Large Crusted Lesions.

stage of the development. The mucous-membrane lesion does not pass through the stage of papule, vesicle, and pustule, but pursues a characteristic course which is determined by its peculiar structure and its different environment. There is perhaps an effort on the part of nature toward the formation of vesicles, but the thin and delicate epithelium which serves as a covering is destroyed by the macerating influence of the moist secretion in which they are constantly bathed. As the eruption upon the skin becomes vesicular and pustular, the lesions in the mouth assume a whitish or grayish appearance, with but little if any elevation above the surface. The denudation of the epithelial covering of the pocks leads to the production of circumscribed erosions or superficial ulcerations.

Soreness of the throat, particularly on swallowing, is one of the most distressing symptoms of the early eruptive stage. But few patients with well-marked attacks escape this suffering. Even when the patient is feeling otherwise well the condition of the throat constitutes a source of bitter complaint. In severe cases, at a later stage, the mucous membrane of the mouth is so abraded, swollen, and painful that the use of solid food is rendered impossible, and the patient is forced to subsist entirely on a liquid diet.

The tongue is often the seat of lesions which seriously embarrass its movement in speaking and eating. Occasionally an intense form of glossitis is set up, causing the organ to swell so enormously as to prevent its retention wholly within the mouth. This condition, which was designated by the older writers as *glossitis variolosa*, is apt to greatly interfere with swallowing, and is under all circumstances to be regarded as an unfavorable sign.

Much annoyance is occasioned by the presence of the eruption in the nasal cavities. The mucous membrane is at first swollen and inflamed, and later covered with crusts which obstruct the nares and render nasal breathing difficult and often impossible. This is particularly a source of distress to nursing infants, who are obliged to release the nipple from time to time to obtain the necessary amount of air.

The eruptive process may involve both the pharynx and larynx and cause so much inflammation and swelling as to make deglutition difficult or impossible, or it may lead to the production of hoarseness and complete aphonia. In severe cases an acute œdema of the glottis may develop, which may seriously or even fatally impede respiration. Trousseau records several fatal cases of this character: "Three smallpox patients, on the eighth day of the disease, which had run a perfectly normal course, were suddenly seized with a fit of suffocation which carried them off in a few seconds, before there was time for anyone to come to their assistance. In one patient autopsy showed laryngitis, with variolous lesions below the glottis."

In severe smallpox in children we have found it necessary in four instances to employ intubation in order to prevent asphyxia. In all of these cases there was laryngitis with considerable swelling of the mucous membrane. Although relief was temporarily afforded, death ultimately

occurred in all four cases. In one of the children the laryngeal stenosis came on late after complete decrustation had occurred on the skin, and at a time when the child appeared to be on the road to recovery.

The mucous membranes of the lower portion of the body may also be involved. The eruption may attack the vulva and the mucous surfaces of the vagina, but the lesions in these parts are not apt to be abundant. The lower part of the rectal mucosa may also be the seat of the variolous eruption. The meatus urinarius is occasionally involved in both males and females, but the urethral channel nearly always escapes.

DELIRIUM.—As previously stated, a variable degree of delirium may accompany the high fever of the initial stage. In our experience the most violent disturbance of cerebration occurs during the early eruptive period. This may be, in some cases, merely the continuation of the earlier delirium, but in others it seems to begin after the exanthem has made its appearance. Some patients are apparently the subjects of delusions of persecution and of hallucinations, and imagine that some one is about to do them bodily harm. Acting on this supposition the demented patient attempts to escape from the hospital and, what is quite strange, will almost always prefer to gain egress through the window. On a number of occasions patients, by the exercise of cunning and the awaiting of a favorable opportunity, have effected their flight with marvellous celerity, and have gained a temporary liberty in this manner. In some patients the temporary derangement takes the form of a suicidal or homicidal mania. One of our patients attempted self-destruction by striking himself on the head with a drinking mug, inflicting several large and painful wounds.

On another occasion a female, by cunningly embracing an opportune moment, quickly ran to an open fire-grate, on which she seated herself. While her clothing was burning around her and her flesh charring, she violently resisted the efforts of the nurse to extricate her. We recall another patient who rose from his bed at night, struck the nurse to the floor, and effected his escape in his night-clothes; he wandered a considerable distance from the hospital, and succeeded, by a shrewd and plausible story, in prevailing upon the credulity of a wagon driver, who conveyed him to his desired destination.

These patients are often able to answer questions coherently, and one, unprepared, may be completely deceived as to their mental condition. They are apt to exhibit, however, some injection of the conjunctivæ and a wild expression of the countenance. This form of delirium was called by the older writers *delirium ferox*.

Patients thus affected require to be closely watched, and, if necessary, restrained in bed by straps or other means. When a patient complains of persecution or asks to be permitted to attend to some business at home for a day or two, close surveillance is necessary.

We have observed this active delirium most often during the papular and vesicular stage of the eruption. When it occurs it is usually associated with the confluent variety of smallpox, yet we have known it to occur in comparatively mild forms of the disease or when the patient

had become quite apyretic. The persistence of the delirium for a number of days is a symptom of evil portent.

The delirium which is seen later, during the decline of the eruption, is of a different character. It is then of a low, muttering form, and frequently associated with general tremor, dry tongue, quick and tremulous pulse, and a collapsed appearance of the features. These nervous symptoms are not peculiar to smallpox, but may be seen in the terminal stage of typhoid and other fevers.

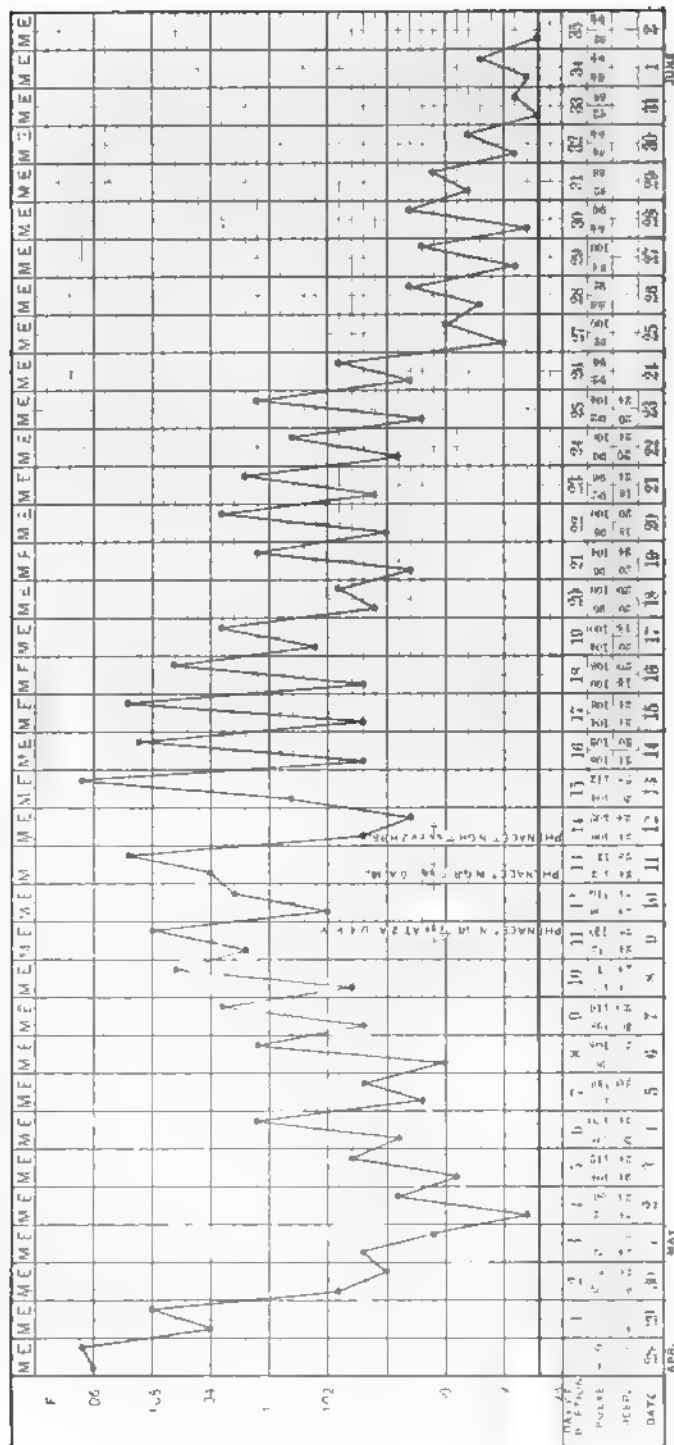
The various forms of delirium, while more frequently observed in alcoholics, appear to be the result of the poison of the disease acting upon the nerve centres.

It has already been stated that the initial *fever* in unmodified smallpox continues high until the third or fourth day of the eruption, when there occurs either a well-marked remission or a brief period of apyrexia. In very mild cases the fever subsides earlier. The fall of the temperature, at this stage, even in severe cases, is not infrequently very rapid, so rapid, indeed, as to drop from a high degree to normal or even subnormal in the course of twelve or eighteen hours. The difference between the morning and evening temperature is not great, although the latter, as a rule, is slightly higher. When the temperature falls there is usually amelioration of all the symptoms. The pulse becomes almost normal; the respirations are easier; the pain in the back, headache, and irritability of the stomach all disappear, except in critical cases; the delirium ceases, enabling the patient to rest and enjoy refreshing slumber. Even the appetite may return, and the patient may be led to believe that the critical period of the disease has passed and that recovery has begun. The subsidence of the symptoms is never so complete in *variola vera* as it is in varioloid. In the latter variety the fever and other systemic symptoms frequently disappear, and the beginning of convalescence is established; but in the former the chief danger is yet to be encountered.

At or shortly after the commencement of the stage of suppuration the temperature again begins to rise, and continues elevated until the completion of the eruptive process, or longer if complications arise. This rise constitutes the so-called *secondary or suppurative fever* of smallpox. This latter pyrexia is not apt to equal in intensity the initial elevation of temperature. When the disease is of moderate severity the temperature may not rise above 102° F. or 103° F., but in well-marked confluent cases it frequently reaches 104° F., rarely exceeding that point. When hyperpyrexia develops, the thermometer registering 105° F., 106° F., or 107° F., the danger of a fatal outcome is correspondingly increased. The maximum degree of fever is often reached during the hours which immediately precede dissolution. Wunderlich reports an antemortem temperature of 109.2° F., and Simon has seen temperatures of 110° and 112° F. immediately after death.

The secondary fever commences ordinarily on the fifth or sixth day of the eruption, when the vesicles begin to fill with pus. It is of indefinite duration, depending directly upon the extent and severity of the

FIG 27



Temperature record of confluent smallpox.

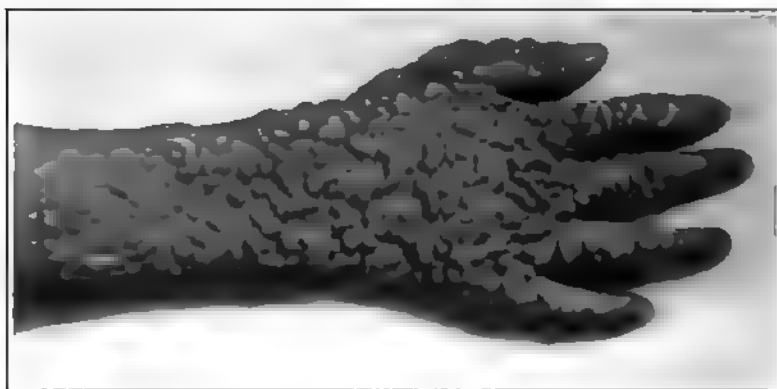
cutaneous outbreak. In a well-marked, discrete, or semiconfluent smallpox the pyrexia is apt to last from three to six days. In severe confluent cases it may continue for eight to twelve days or longer. It is not uncommon for the secondary fever to merge without intermission into the pyrexia produced by the common septic complications, such as boils, abscesses, etc. The elevation of temperature may, under such conditions, continue for four, five, or six weeks or even longer. In the beginning of the suppurative fever the variation between the morning and evening temperature is apt to equal one or two degrees. The maximal elevation usually occurs, in severe cases, between the seventh and tenth days. Later, when boils and abscesses develop, the diurnal variations are most pronounced, the evening fever not infrequently reaching 104° or 105° F., while the matinal temperature registers only 99° F. The pulse and respiration correspond in a general way with the temperature curve. The pulse, however, is apt to be higher in proportion to the temperature than during the initial stage. With a temperature of 104° or 105° the cardiac pulsations not infrequently reach 140 or 150 to the minute. When the morning remission occurs there is a considerable slowing in the pulse rate. As is quite to be expected, the patient experiences more comfort in the mornings than later in the day. During the pustular stage the chief complaint of the patient is the general soreness of the skin. The couch upon which he lies is metaphorically, if not actually, "a bed of thorns;" whichever way he turns he makes pressure upon the sensitive and inflamed pocks. Nervous apprehension, restlessness, and sleeplessness are prominent symptoms of this period. The patient is conscious of an increasing degree of prostration, and is frequently much concerned as to the outcome of the illness. It becomes necessary to allay the nervousness of the patient and induce sleep by the administration of an anodyne. At the end of the eighth or ninth day a sudden improvement in the general condition of the patient is often observed. The sufferer becomes brighter, volunteers information that he feels better, and exhibits altogether a lesser degree of prostration. This is usually coincident with the onset of the period of involution and retrogression of the eruption.

Period of Involution and Retrogression of the Eruption.—The exanthem of smallpox reaches the acme of its development with the completion of the pustular stage. This constitutes the turning point not only of the eruption, but frequently of the disease. The first evidence of retrogression of the exanthem is noted in the subsidence of the inflammatory swelling of the skin, more particularly in the immediate neighborhood of the pustules. The abatement is first seen on the face, where the redness and œdema have been most conspicuous. The eyelids become less swollen, permitting the patient to again perceive the grateful light of day. The tumefied features gradually assume their normal contour, and the patient begins to acquire some semblance of his former self. Synchronous with the disappearance of the intumescence the pustules begin to dry; this period is called, therefore, the *stage of desiccation*. The drying of the contents of the pustule is soon followed by

a casting off of the crusts, when the *stage of decrustation* is entered upon. Nature in this manner attempts to rid the surface of the skin of the effete products which have there collected, and, finally, restore it to its normal condition.

The involution of the smallpox exanthem does not occur simultaneously upon all portions of the body surface, but follows the same sequence observed during the development of the eruption. It is but natural, therefore, that the first evidence of desiccation should be found in the facial lesions. The pustules in this region may dry without rupture, although more commonly the purulent contents of the lesions exude upon the surface and dry in the form of yellowish crusts. This color gradually becomes darker until it assumes a brownish tint. In neglected cases the crusts may become almost black, enveloping the face in an unsightly, immovable mask. The adherence of the crusts to the subja-

FIG. 28



Unusually large and confluent pustules on the ninth day of the eruption

cent tissues varies in degree according to the depth and intensity of the involvement of the cutis. Where the pustule is superficially seated and there is no ulceration of the skin, the crust is readily detached, exposing to view merely a reddened area of the skin.

At the same time that desiccation is well established on the face, the trunk and extremities will exhibit lesions distended with fluid pus. These rupture, form crusts, and then pass through the process just described. At this period of the disease the offensive odor previously mentioned becomes most marked; in some cases it is quite unbearable, especially when the contents of the pustules discharge and decompose on the skin, or soak into the bed-clothes and there undergo putrefaction.

After the rupture of large pustules the centres frequently dry and sink in, producing a cup-shaped depression or umbilication. This *secondary umbilication* differs from the primary variety in being distinctly larger, more conspicuous, and occurring at a much later stage of the eruption. This form of umbilication is most typically seen on the dorsal surfaces of the hands.

PLATE XX.



Smallpox in the Late Pustular and Desiccative Stage.

Arms and hands show secondary umbilication due to rupture and central collapse of pustules.

When the variolous pocks desiccate without rupture they undergo a gradual condensation of structure and a deepening of their color. When they are completely dried they are convexly flat, rounded, of horny hardness, and of a characteristic reddish-brown or mahogany color. Upon the back of the hands the dried, horny pock not infrequently preserves in its centre a well-marked umbilication. Some of the crusts exhibit peculiar markings resembling an x or a maltese cross. In severe smallpox these horny pocks are usually limited to the hands and feet. In varioloid they may develop in other regions also, even upon the face. In this case the pustule, which is usually small, contracts into a hard, horny, shining crust of a reddish-brown color. These crusts are often of diagnostic value, particularly when mild cases are seen at a late stage of the disease.

FIG. 29



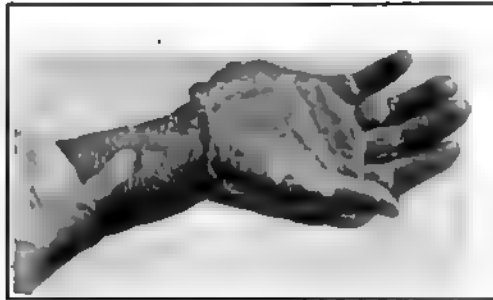
Dried pocks embedded in the horny layer of the palms of the hands.

Upon the palmar and plantar surfaces the smallpox lesion dries into the mahogany-colored crust described. These pocks have the shape of lentil seeds, and are embedded in the thick, corneous layer of the epidermis. Here they remain for weeks if undisturbed, becoming denser in structure and darker in color. But few patients have the patience to wait for the spontaneous shedding of these crusts. It is a favorite occupation of convalescents to shell out the dried pocks from their epidermal beds. Inasmuch as the pocks in this region usually have their seat in the epidermis, nothing is left save small excavations in the horny layer. The uppermost layer of the epidermis is later removed through the process of desquamation. The mahogany-colored pocks upon the palms and soles present a quite characteristic appearance, which may render aid in the diagnosis in doubtful cases. In very mild cases minute pocks not larger than pinheads are found interspersed with the larger lesions.

The stage of desiccation usually begins about the eleventh or twelfth

day of the eruption; in mild cases it commences earlier, while in grave forms of the disease it is postponed. If the case is to end in recovery there is at this time, not only improvement in the cutaneous symptoms, but also an amelioration in the general condition of the patient. With

FIG. 30



Exfoliation of the palmar epidermis containing embedded pocks occurring in the later stage of severe smallpox.

FIG. 31



Soles of feet from which the hard, embedded pocks have been removed

the involution of the exanthem, the fever subsides and the pulse lessens in frequency. In favorable cases the temperature each day more nearly approaches the normal standard. If there be considerable involvement

of the skin and mucous membranes the temperature falls less rapidly, or if complications arise it continues for a varying period according to the nature of the associated conditions. Although the fever is steadily decreasing, the patient is still in danger from exhaustion, for the heart, kidneys, and other organs have been severely taxed by the septicæmic poisoning.

The mucous-membrane lesions of the upper air passages improve in favorable cases at a rather earlier period than the cutaneous manifestations. The distressing pain on swallowing has often disappeared by the sixth day. The nasal, buccal, and pharyngeal eruption, being less deep and destructive, undergoes a comparatively rapid involution.

In regular cases of *variola vera* it usually requires, after desiccation has commenced, from three to four weeks for all of the crusts to become detached and fall off. This makes the entire duration of the disease about five or six weeks.

FIG. 32



Well-pronounced discrete smallpox; clustering of lesions due to previous abrasions at such sites.

During the drying stage a new symptom is added to the sufferer's already extensive category of ills. The incrustation of the pustules is accompanied by the development of *itching* which varies in intensity from slight annoyance to unendurable distress. Adults are usually enabled to restrain themselves from scratching by the exercise of self-control. Children, on the other hand, yield to the impulse to purchase relief by scratching or rubbing, with the result that injury is often inflicted upon the skin. It is not uncommon to see in children, who have had unbridled license in the use of their hands, large, abraded, bleeding surfaces or crusted sores where the pustules have been gouged with the finger-nails. It is popularly believed that the scarring in smallpox is due to secondary injury from scratching. While this agency may be a factor in the production of a few of the cicatrices, the vast

majority of them result from the destruction of portions of the corium by the variolous inflammation. That finger traumatism plays but an inconsiderable role in the scarring is evidenced by the fact that children, despite the mechanical violence which they inflict upon the skin, escape as a rule with less disfigurement than adults. This is doubtless due to the fact that the pocks in children are more superficially situated in the integument. The most serious consequence of scratching is in the increased liability to pyogenic infections of the skin and the subcutaneous tissue.

It is only after the completion of the decrustation that one can determine the extent of permanent injury to the skin. If the crusts have been softened off by unguentous substances or mechanically removed, small, irregular depressions filled with granulating tissue show where the integrity of the papillary layer of the skin has been affected. On the spontaneous shedding of the crusts these areas will be seen as reddish, cicatrized excavations. The extent of scarring depends entirely upon the depth to which the destructive inflammation has extended. Pocks which remain encapsuled within the epidermis will leave no permanent evidence of their presence. They will be followed by reddish stains, the result of a passive hyperæmia of the papillary bloodvessels. These discolorations are quite disfiguring in themselves, but disappear in the course of a few months. On exposure to cold the reddish stains acquire a bluish or purplish appearance. As time goes on the reddish color becomes darker and eventuates in a brownish *pigmentation*. This pigmentation is fortunately less conspicuous and less persistent on the face than on the covered surfaces. Even after several months the trunk and limbs frequently exhibit stains of a *café-au-lait* hue. In persons of swarthy complexion and in negroes the pigmentation is greater than in fairer-skinned individuals. The stains in the African race are often quite black and appear to persist longer on the face than in Caucasians. Where the true skin has been destroyed in negroes, the normal pigment of the skin is frequently lost. In such cases a whitish or pinkish discoloration is seen in the centre of the scar, with a hyperpigmented zone surrounding it.

After the lapse of three or four months the *scars* of smallpox assume a whitish color, paler, indeed, than the surrounding integument. They may be round, oval, linear, stellate, radiate or irregular, according to the configuration or grouping of the lesions which caused them. They may be large or small, deep or shallow; not infrequently they present sharp, overhanging edges. Indeed, there is nothing specially characteristic about the pits left after variola, save their extent and distribution. Affecting most profusely and conspicuously the face, they give rise to the well-known "pock-marked" countenance. It is well to remember, however, that similar pits sometimes follow a severe acne, particularly of the necrotic type. The writers have seen scarred acne patients who might have passed for variola subjects. The older writers gave to acne the significant title of "stone pock."

By a curious irony of fate, nature obliterates the remains of the vast

PLATE XXI.



Severe Attack of Smallpox in an Unvaccinated Woman. Tenth day of Eruption. Face painted with tincture of iodine.

PLATE XXII.



Pigmented Stains following a Severe Attack of Smallpox.

majority of variolous lesions upon the covered surfaces of the body, whereas indelible evidence is left upon the face and frequently the hands to bear witness to the cruel disease through which the patient has passed. Time, however, accomplishes much toward the effacement of the more superficial scars and the mitigation of the disfigurement produced by the deeper cicatrices.

The hair of the head, beard, eyebrows, etc., may be lost after the termination of a severe smallpox, especially in cases in which the eruption has been profuse in these areas. This *alopecia* is probably in part of febrile origin and partly the result of the local influence of the exanthem. Restoration of the hair usually occurs, and this is complete

FIG. 38



Deep scarring and temporary loss of hair after recovery from confluent smallpox.

except in areas in which the hair papillæ have been destroyed by the variolous lesions.

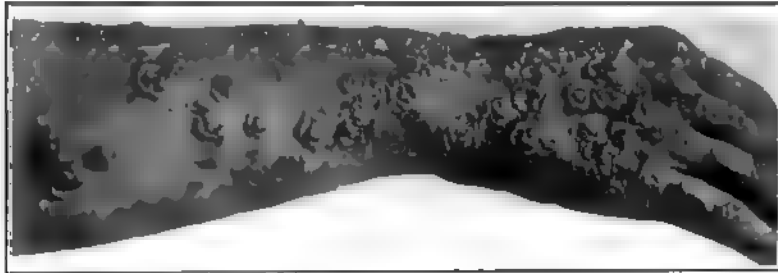
The *nails* of the fingers and the toes may be shed in severe cases. This is usually accomplished slowly through the pushing off of the old nail by the new one growing from behind. After six or eight weeks a sharp, elevated ridge is seen near the nail fold; this represents the free border of the new nail, which in the course of time extends forward. Not infrequently variolous lesions are located beneath the nail. These *subungual pocks* are of a purplish or reddish-brown color, looking not unlike traumatic ecchymoses.

When convalescence sets in in uncomplicated cases, improvement in

the general condition of the patient is rapid. The appetite returns and is apt to become keen, sometimes even voracious. The digestive functions are active and the patient rapidly regains strength and weight.

Impetigo Variolosa.—During the period of desiccation and incrustation in smallpox certain secondary changes commonly occur upon the skin. One of these is the development of sparsely distributed blebs containing a thin, dirty-yellow fluid. These may originate in several distinct ways. They may spring up upon previously healthy inter-pustular areas of skin, or they may result from a direct conversion of the pustules into blebs. At times a pustule is seen one-half of which is still yellowish, while the other half is spreading out into a muddy-colored bleb. The blebs are commonly flat, although at times they rise prominently from the surface; they vary in size from a bean to a walnut. The epidermal roof is flaccid, wrinkled, and thin, and easily disposed to rupture, when a thin, yellowish fluid exudes, which dries in the form of irregular crusts. This form of bleb formation is most frequently seen on the hands and feet, where they may reach a diameter of an inch or more.

FIG. 34



Variolous impetigo, showing undermining of the epidermis around the dried pocks; appearing during the decline of the eruption.

A more common change in the pustules, however, is the development around the partially desiccated crust of a reddish, vesicular ring, containing a turbid, puriform secretion; just beyond the border of the raised-up epidermis is a narrow, pinkish band, which indicates the spreading edge. These flat, bullous patches spread peripherally, lifting up the epidermis as extension takes place, until perhaps an area the size of a silver half-dollar is reached. Central crusting proceeds concurrently with centrifugal extension. In this manner large, dirty-yellow, irregular, friable crusts are formed. It is not uncommon for most of the pustules on the trunk and extremities to become surrounded by a spreading, vesicopustular ring, producing an extensive secondary eruption. Nearly all patients with unmodified smallpox present these "sores" upon the skin. Where the eruption is profuse there may be considerable elevation of temperature and other evidences of septi-cæmia. Indeed, this extensive secondary skin involvement may even cause death.

One of the patients at the Municipal Hospital, a woman aged sixty

PLATE XXIII.



Extensive Impetigo Variolosa following a Moderately
Severe Attack of Smallpox.

years, was apparently recovering from smallpox when an extensive outbreak of the character described developed and led to a fatal termination. The crusts in this case were numerous and voluminous and left, after removal by unguentous applications, large areas of denuded skin.

The various forms of pustulo-bleb formation just described are so common in smallpox that this complicating condition might appropriately be designated *impetigo variolosa*. Indeed, this term was employed by Hebra¹ for one of the forms of bleb formation above referred to. In 1867 he wrote: "In other instances a consecutive suppuration appears, not round crusts formed from variolous pustules, but in the intervening spaces which were free from the efflorescence. Thus, there appears a second pustular eruption, which might almost be regarded as a second smallpox eruption, were it not that the pustules have a different form, and take a different course. In fact, they resemble

FIG. 35



Impetigo variolosa complicating a severe attack of smallpox

rather those of the common pustular affections, and therefore this affection may be called *impetigo variolosa*." Hebra preceded this description by a reference to "central crusts with small vesicular rings, containing a puriform fluid," to which he applied the name *rupia variolosa*.

Microscopic and cultural examination of the contents of variolous vesicles and pustules demonstrates that the ordinary pyogenic organisms are absent in the early stages of the lesions, but commonly appear during the late pustular period.

In a bacteriological study of the vesicles and pustules of smallpox² we found the lesions to be sterile until a late stage of the eruption.

¹ *Diseases of the Skin*, Translation of the New Sydenham Society, p. 251

² Schamberg Preliminary Report of a Study of the Contents of the Vesicles and Pustules of Smallpox, *Journal of the American Medical Association*, February 14, 1903

Of 34 cultures of fluid from variolous lesions before the seventh day of the eruption, 33 remained sterile. And even on the eighth, ninth, and tenth days bacteria cultivable on ordinary media are not infrequently absent. Of a total of 82 cultures made, 64, or 77 per cent., failed to show any growth whatsoever. Frequently, thick, creamy pus was deposited upon nutrient media without giving rise to any colonies whatsoever. These results, which are in accord with most similar investigations, suggest that the *causa causans* of smallpox, which is, of course, resident in the lesions, is itself pyogenic, and that it is responsible for the suppuration of the variolous pock. Suppuration is, therefore, to be regarded as a part of the normal evolution of the eruption of smallpox. After the eighth or ninth day of the eruption, however, it would appear that a secondary infection, with germs commonly present on the skin, takes place. At this time variolous impetigo develops. The thin, seropurulent fluid in the impetigo blebs, when examined in smear, is seen to contain myriads of micro-organisms, chiefly streptococci, although staphylococci and a pseudodiphtheria bacillus are also found. Cultures of this fluid or of the material from the flat impetigo lesion around the variolous crusts, invariably give rise to growths of these several organisms alone or combined. Fluid from a large bleb was injected beneath the skin of a dog; in a few days a local tumefaction the size of a walnut developed, which became surmounted by a dime-sized bleb. This ruptured and left a superficial ulceration. The swelling disappeared and recovery occurred without any further local or general symptoms. When death occurs in smallpox, streptococci may, in the vast majority of instances, be recovered from the heart and other internal organisms. Most of the deaths in smallpox occur from septicæmia from the ninth to the eleventh day of the eruption.

As is well known, the commonest complications of smallpox are boils and subcutaneous abscesses. Seldom does a well-marked case of variola vera finish its course without being accompanied by furuncles and phlegmonous infiltrations. We have been impressed with the fact that the tendency to these complications is increased by a pre-existent severe variolous impetigo.

Cutaneous gangrene occasionally occurs during the course of smallpox; we observed this complication about a half-dozen times in the Municipal Hospital during the recent epidemic of 1901-'04. These cases are commonly preceded by an extensive impetigo variolosa. Fig. 36 shows a patch of gangrene on the inside of the thigh in a patient who had a severe impetigo. This patient was desperately ill with septicæmic symptoms, but ultimately recovered.

The statement appears to be justified that impetigo variolosa increases the liability to the deeper pyogenic infections, such as boils, abscesses, erysipelas, and cutaneous gangrene. It, moreover, appears to bear a relationship in many cases to the development of certain postvariolous rashes presently to be described.

It has been our practice at the Municipal Hospital to give antiseptic

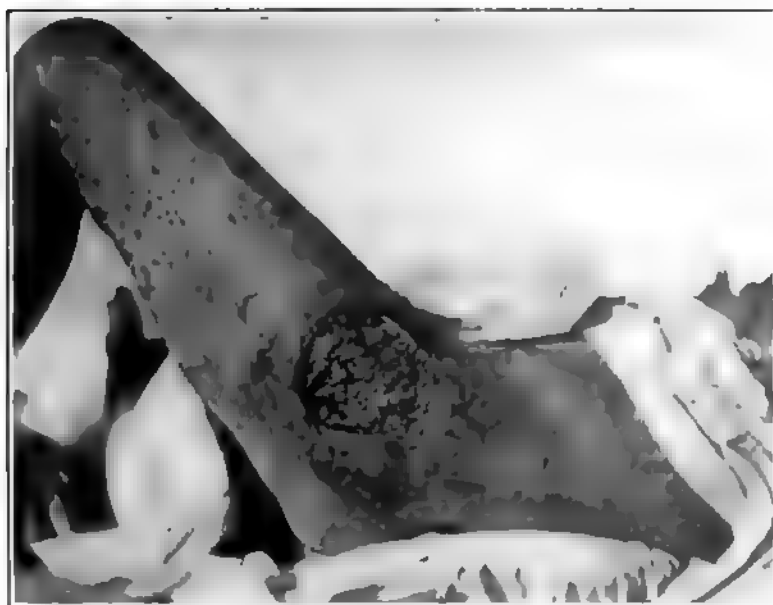
baths to smallpox patients during the late suppurative stage of the disease. The patient is immersed for fifteen or twenty minutes in a bath consisting of a 1 : 10,000 to 1 : 20,000 solution of corrosive sub-

FIG. 36



Gangrene of the skin complicating severe smallpox ; recovery.

FIG. 37



Gangrene of the skin accompanying a severe smallpox ; ultimate recovery.

limate. In other cases we have employed a 1:500 solution of creolin. After the bath the patient is dusted with weak antiseptic powders. This course of treatment has a beneficial influence in drying up the impetigo sores and in lessening the tendency to deeper infection.

Secondary Toxic or Septic Rashes.—Another secondary eruption in smallpox, to which but little reference has been made in literature, is the toxic or septic rash which appears in a certain percentage of cases during the stage of decrustation. Between the eighth and eighteenth days, and most commonly on the thirteenth or fourteenth, there develops upon the trunk, extremities, and at times the face, a peculiar erythematous efflorescence. In most instances the rash consists of a diffuse, dusky redness bearing a strong resemblance to the exanthem of scarlet fever (*scarlatiniform erythema*). At times it is mottled and inclined to become somewhat morbilliform in appearance. The scarlatiniform eruption is peculiar in that the skin immediately surrounding the drying pocks is often exempted, producing a sort of anæmic halo. The rash lasts for two or three days and then fades away. If the erythema has been well marked it is prone to be followed by desquamation, which may be most profuse in character. The exfoliation of the epidermis is usually rapid, and may be out of proportion to the intensity of the rash. Fig. 78 shows desquamation of the cuticle of the palms in large masses on the sixth day of the rash. In this patient the eruption was quite indistinguishable from that of scarlatina. In occasional instances a most inordinate and persistent desquamation follows. A young lad developed on the fourteenth day of the smallpox eruption a severe, deep-red erythema, which was followed by repeated exfoliation of the epidermis. This patient desquamated four or five distinct times, the whole process extending over a period of six or eight weeks. Handfuls of scales could be daily gathered from his bed. The hair of the scalp and eyebrows, and the finger-nails were subsequently lost. A patient recently in the hospital passed through an almost identical attack. Such cases merit the designation of *dermatitis exfoliativa variolosa*.

In rare instances these secondary rashes may become hemorrhagic. Hæmic extravasation into the skin is most apt to occur upon the lower extremities, where the stasis in the vessels is greater owing to gravity.

We have seen a severe secondary *purpuric rash*, the history of which is of sufficient importance to warrant its presentation:

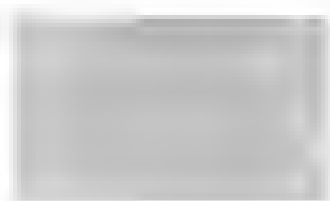
H. W., an unvaccinated boy, aged seven and a half years, was admitted to the hospital on September 28, 1901, on the fourth day of the smallpox eruption. The attack was severe, the eruption being semiconfluent. The patient did well for seven or eight days. On the thirteenth day of the eruption, the face, on which the swelling had largely subsided, again became tumefied, the temperature rose, and a profuse macular eruption, rapidly becoming purpuric, and consisting of bluish-red pin-head to finger-nail-sized ecchymoses, developed over the trunk and extremities. The patient sank rapidly and died in two days.

The secondary rashes are not infrequently accompanied by rise of temperature. The temperature may suddenly mount to 104°, decline

PLATE XXIV.



**Exfoliative Dermatitis Occurring during the Course
of a Severe Smallpox.**



11

rapidly, and then remain for some days in the neighborhood of 101° or 102° F. In some patients, with rashes of moderate severity, no pyrexial elevation occurs. While the eruption lasts the patients are, as a rule, somnolent, extremely irritable, and considerably prostrated. The rashes are more commonly observed in patients who have had severe smallpox eruptions.

During the epidemic of 1901-03, we observed these eruptions in perhaps 5 per cent. to 8 per cent. of all patients admitted. The incidence among children seemed to be greater than among adults. In the severe epidemic of smallpox in 1871-72, such rashes were much less frequently observed, and in the year 1904 they were distinctly less frequent than in the two preceding years.

The scarlatiniform eruption is the type by far most commonly seen. The resemblance to the rash of scarlet fever is so strong that in the beginning the existence of the latter disease was suspected. In a smallpox hospital in a neighboring town, several patients with scarlatinoid rashes of the character referred to were believed to be suffering from scarlet fever and were promptly isolated. The physician, during a visit to our wards, identified the toxic rashes with the eruption he had observed.

Perhaps some of the cases of scarlet fever associated with smallpox reported by the older writers were in reality instances of scarlatiniform erythema.

In a boy recently treated in the hospital, a severe variolous impetigo developed, and this was followed on the fourteenth day of the smallpox eruption by an intense *maculopapular rash*, which was on the trunk quite indistinguishable from measles; on the face, however, there was relatively little eruption. The duration of the eruption was brief, and catarrhal symptoms were absent.

The postvariola rashes are in all probability septic or toxic in character, due doubtless to the absorption of some poison into the blood. Our experience in the Municipal Hospital would indicate that these are more common in patients who have been the subjects of an abundant impetigo.

As far as we have been able to ascertain, none of the modern textbooks or monographs on smallpox, save the article by Moore, make mention of these rashes. The earlier writers doubtless regarded the development of the erythema as evidence of an intercurrent scarlet fever, and the numerous instances of the coincidence of these two diseases may thus be accounted for.

Simon,¹ in an article on scarlatina and scarlatiniform eruptions in the course of smallpox, written in 1873, carefully distinguished these two conditions and reported cases representing both true scarlet fever and the secondary erythema which resembles it. In the latter cases he considers the diagnosis of scarlet fever excluded by the date of onset of

¹ Ueber Scharlach und Scharlach-ähnliche-ausschläge im Verlauf der Variola, Archiv f. Dermatologie u. Syphilis, 1873, p. 115.

the complication, the absence of adequate invasive symptoms, the mild character of the angina, the absence of or slight character of the desquamation, and the non-contagiousness of the condition.

Of thirteen cases of secondary rash, Simon observed nine develop after the tenth day of the variolous eruption. A few were seen as early as the sixth day and as late as the eighteenth or twentieth day. Simon does not seem to have encountered the profuse desquamation which has occurred in some of our cases. No mention is made by him of morbilliform rashes.

According to Simon, Fleischmann also saw some of these cases, as did likewise Bernouilli, who states that in 1865 he saw a case of secondary erythema in variola which he erroneously regarded as an intercurrent attack of scarlet fever.

The only other reference to these rashes that we have been able to find is by Meredith Richards,¹ Medical Officer of Health of Chesterfield, England. This writer refers also to the bullous and pustular eruptions occurring late in the course of variola. He says:

“Less known, and from a practical point of view less important, are certain posteruptive rashes, which include (1) a scarlatiniform erythema, general in distribution, and not differing from that common in various septic states; (2) a development of the smallpox pustules which appears to correspond to what Dr. Crocker has recently described as “*impetigo contagiosa gyrata*.” The smallpox pustules, instead of drying up and scabbing on the eleventh day, show signs of spreading peripherally, so that in a day or two many of the lesions consist of three well-defined parts, viz., a central scab, a surrounding vesicular ring which rapidly becomes pustular, and a red areola surrounding the pustular ring. Unless treated, the areola and pustular ring continue to spread centrifugally until the whole lesion may measure an inch or more in diameter. When abundant, this rash gives rise to a very remarkable appearance, and is clinically important because it is often attended by high temperature and other signs of septicæmia. There is no doubt that this is due to a mixed infection, as it has a tendency to occur in particular wards and may be accidentally acquired by attendants. It also merits notice in passing, as, I believe, this variety of secondary infection has not been fully described. (3) Accompanying the previous rash or occurring in other cases exhibiting signs of septicæmia, it is not infrequent to observe cases in which the healthy interpustular epidermis is raised into flaccid bullæ, containing a few drops of foul, mucopurulent fluid. These bullæ are soon followed by profuse desquamation, which may lead to the shedding of the nails, and are accompanied by severe constitutional symptoms of a septicæmic character. Many of them are fatal, though a good proportion appear to owe their lives to boracic baths combined with good nursing and general tonic treatment.”

¹ Accidental Rashes Occurring in the Course of the Exanthemata, *Quarterly Medical Journal*, 1896, p. 31.

PLATE XXV.



Confluent Variola on the Fourteenth Day of Eruption, showing a Collapsed Condition of the Pustules and Commencement of Desiccation.

THE VARIETIES OF SMALLPOX.

The course just described relates more particularly to that form of the disease in which the eruption is either *discrete* or *semiconfluent*. In our experience the vast majority of cases met with belong to the last-named variety—that is to say, the eruption is usually either partially or wholly confluent on the face, the dorsal surfaces of the hands, and the lower portions of the forearms, while on the trunk and extremities it is discrete, save a few lesions, perhaps, which may coalesce. Variations in the extent of the eruption may reach extreme limits, from a few small pustules, scarcely characteristic enough to enable one to definitely proclaim the variolous nature of the disease, to the most extensive eruption covering the entire cutaneous surface. Between these two extremes there may occur numerous grades of intermediate severity.

Confluent Smallpox (Variola Confluens).—It can hardly be said that there is any symptom during the initial stage of smallpox peculiar to the confluent form of the disease. Inasmuch, however, as the symptoms preceding this type of variola are, with great uniformity, of a severe character, this grave form may be excluded in the presence of mild initial manifestations. Most prominent among the early symptoms are severe headache, persistent retching and vomiting, delirium, or, in children, stupor, violent pain in the back, and high fever. The temperature always rises rapidly, and attains frequently an extraordinary height. It is not at all uncommon for the fever to reach 105° or 106°, F. and cases have been recorded in which a temperature of 110° F. was registered. On the third, fourth, or fifth day of the eruption the temperature declines, but this remission is never as complete as in milder cases, nor does it continue as long. During the remission the temperature is not far from 101° or 102° F., at which point it is apt to remain for a period of two or three days, when the secondary rise commences. The fever, during the stage of suppuration, is not usually as intense as in the initial stage, yet it may at times rise considerably higher. The chart shown upon page 184 illustrates the temperature curve of a severe case of confluent smallpox, and may be taken as a fair type of the cases of this class. It may be well to add that the temperature in the suppurative stage was somewhat influenced by the use of antipyretics.

It is sometimes stated that the eruption of confluent smallpox develops early, often on the second day of the initial fever. Our experience leads us to believe that this variety develops less rapidly than in modified forms of the disease, but there is a shorter interval between the time of its appearance on the face and on other portions of the body. So quickly is the eruption diffused over the whole body that it has been mistaken in the papular stage for measles. Indeed, it is the confluent form of variola which is particularly apt to be confounded with morbilli. Ordinarily in forty-eight hours the efflorescence has covered the entire body surface. Owing to the extensive involvement of the skin, redness and swelling begin early. The face is intensely hyperæmic and the seat of distressing burning and itching. The marked suffusion

of the countenance frequently enables one to prophesy that the disease will take the confluent form. As the eruption progresses it passes through the usual stages, though somewhat more slowly than in the milder cases. The papules are thickly set, and even at this stage a coalescence of lesions may be noted. The skin is thickened and indurated, and feels like embossed leather. Soon the grayish outlines of the vesicles make their appearance and the confluent aspect of the exanthem becomes accentuated. With the conversion of the vesicular contents into pus, great swelling and cedema develop, particularly about the face and scalp. The eyelids are enormously puffed, and the margin of the upper lid so greatly thickened that it completely overlaps the lower. The nose, lips, and ears are swollen and distorted, imparting to the countenance a most hideous expression. The transformation of the features is so rapid and complete that nurses and physicians who are off duty for a day or two are frequently unable to identify such patients on their return to the wards. The hands and feet are swollen

FIG. 38



Profuse eruption upon hands.

to double their natural size, and are most exquisitely tender and painful. When full pustulation is established the neighboring lesions coalesce and form large, flat blebs. In severe cases the walls of the pustules are completely swept away, producing flat, purulent, pasty-looking infiltrations of enormous proportions. When the pus exudes upon the surface and dries, a most disgusting stench arises from the body.

In favorable cases, with the beginning of desiccation, a subsidence in the cedema takes place, and the crusts are cast off from the skin. The decrustation is, however, slower than in the discrete and semiconfluent forms of the disease. The suppurative process is deeper and more persistent, and may lead to the consecutive production in the same areas of large crusts which are successively thrown off as they form. Owing to the greater depth of the purulent inflammation in the integument, more extensive destruction of the true skin occurs and consequently the scarring is deeper and more conspicuous. Instead of discrete pits the face may be seamed with scars in a most frightful manner.

In severe cases which are going to terminate fatally the course pursued is rather different from that above described. The evolution of the eruption is excessively slow, the lesions appearing to be suppressed and accompanied by but little swelling. The face has a peculiar blurred appearance. The older writers regarded the swelling of the face as a favorable sign, inasmuch as it indicated a certain vigor of the constitution. Physicians who have had experience with smallpox will recognize the correctness of this observation. Swelling of the features is to be welcomed as a favorable indication, and the absence of œdema in confluent eruptions must be regarded with grave foreboding. An ominous sign in these cases is the early development of flat, brownish, depressed scabs on a few of the vesicles on the forehead and cheeks. In these suppressed eruptions the vesicles are only partially filled with fluid, and the features are only slightly swollen; the skin is roughened and presents a somewhat parchmenty appearance. There is most profound prostration, and death results in almost every case.

FIG. 39

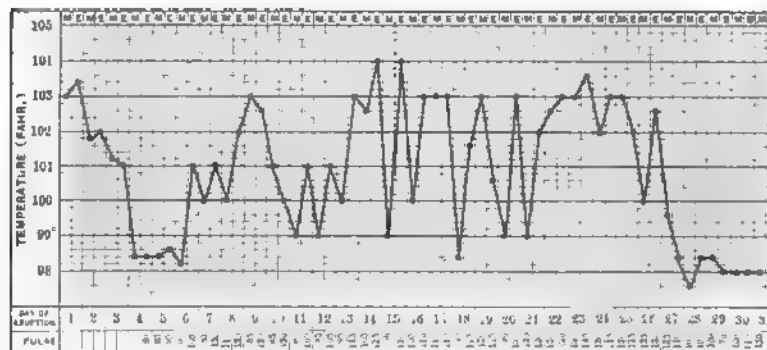


Swelling of the face on the seventh day in a fatal case of smallpox.

In confluent smallpox the mucous membrane of the mouth, throat, and nose is always severely involved. The epithelium of these parts frequently becomes so completely disorganized by the eruptive process that it presents the appearance of diphtheritic membrane. Swelling of the tonsils and soft palate is often so great as to cause the greatest difficulty in swallowing. It is in the intensely confluent cases that *glossitis variolosa* is apt to occur. The parotid gland sometimes becomes acutely inflamed, perhaps by extension along the ducts of Steno. Profuse expectoration of saliva is not infrequently noted. The pharynx and larynx are almost always the seat of an extensive eruption, giving rise to dysphagia, hoarseness, and aphonia. Acute œdema of the glottis is one of the most serious accidents to which this form of the disease is liable; when it develops the patient's life is placed in imminent danger. At a somewhat later period serious submucous infiltrations of pus may develop, producing tonsillar or postpharyngeal abscesses or perichondritis of the larynx.

The constitutional symptoms during the suppurative stage of confluent variola are most pronounced. There is marked pyrexia (104° to 105° F.), rapid pulse, frequent cough and expectoration, great restlessness, inability to sleep, and profound prostration. Delirium is very common, but the patient does not become maniacal as he often does earlier in the disease. At this stage, also, complications are liable to occur, such as corneal ulcer, keratitis, pleurisy, empyema, suppuration of the joints, cellulitis, phlegmonous inflammations, and gangrene of the skin. Vomiting and diarrhœa may supervene, and still further exhaust the patient's ebbing vitality. In fatal cases the patient sinks into a comatose condition, the pulse becomes excessively rapid, and the temperature not infrequently rises to 105° , 106° , or 107° F. Thus closes the final chapter in one of the most distressing, cruel, and frightful diseases "to which human flesh is heir."

FIG. 40



W. F., aged thirty-seven years. Case of smallpox in an unvaccinated man, showing the rise of temperature in the initial stage, the secondary or suppurative fever, and a later irregular fever due to abscesses and cellulitis, recovery.

The mortality rate in confluent smallpox varies in different epidemics, but it is always extremely high. In general terms it may be stated that at least one-half of such cases perish. When this form of the disease terminates in recovery it is only after a long and tedious convalescence, interrupted by the development of boils, abscesses, and other complications.

Hemorrhagic Smallpox.—Of all the forms of variola the hemorrhagic is the most formidable and malignant. For those who contract a well-marked attack of this type of the disease there is absolutely no hope.

According as the hemorrhage precedes or follows the appearance of the variolous lesions, two varieties are distinguished. (1) the so-called *purpura variolosa*, in which the hemorrhage is the primary exanthem; (2) *variola pustulosa hemorrhagica*, in which it comes on secondarily.

In certain epidemics a petechial eruption is frequently seen at the close of the initial stage of the disease, at or about the time when the eruption should appear. This symptom often precedes the purpuric

PLATE XXVI.



Hemorrhagic Smallpox in a Puerperal Woman.

Cutaneous surface covered with petechiae and ecchymoses. A few
ill-formed papules were present.

or hemorrhagic form of the disease, and is therefore, as a rule, an early sign of malignancy. At other times petechiæ and ecchymoses appear between the papules or vesicles, or develop actually in the bases of these lesions. The vesicles and pustules may contain purulent material or may fill up with sanguinopurulent fluid. Considerable diversity of appearance is sometimes manifested in the eruption of a single case.

There is no satisfactory explanation at hand to elucidate the causation of hemorrhagic smallpox. It would appear that the determining factor is largely resident in the individual, inasmuch as such cases may be derived from ordinary smallpox, and, on the other hand, may give rise to the usual forms in other people. The frequency of this form of the disease varies in different epidemics, being commonest when a more malignant type of the disease prevails. It is well known, for example, that hemorrhagic variola was exceptionally common during the virulent pandemic of smallpox in 1871-72.

Variola Purpurica.—*Variola purpurica*, or *purpura variolosa*, is the gravest and most malignant form that smallpox can assume. Zuelzer has called attention to the observation that the period of incubation in hemorrhagic smallpox is not infrequently abridged to six or eight days. The initial stage does not differ essentially from that of ordinary variola. The patient suffers from chill, fever, and headache, although the temperature is not as likely to reach so extraordinary a height as in confluent smallpox. The pain in the back is usually violent, and prostration excessive. Furthermore, the patient often suffers from precordial distress, and from severe retching and vomiting. The vomiting in this form of the disease is a most distressing symptom, and commonly proves more persistent than in ordinary smallpox. It not infrequently continues for several days after the appearance of the exanthem. Toward the end of the initial stage a diffuse efflorescence appears on various parts of the trunk and extremities, while the face remains for a time exempt. The rash is at first scarlatinoid in appearance, and disappears partially under digital pressure; later it becomes more intense and of a deeper hue, and hemorrhagic extravasation into the skin occurs. Petechiæ, vibices, and ecchymoses develop upon the chest, axillæ, lower portion of the abdomen, the groins and legs; the dark-red or purplish discoloration now present no longer fades away under pressure of the finger. The discoloration rapidly extends to the face, which becomes dusky red or livid and swollen. The conjunctivæ are injected, the eyes bloodshot, and the lids bluish, owing to hemorrhage into the cellular tissue. Frequently the extravasation of blood under the conjunctiva covering the sclerotica is so great as to cause this membrane to project beyond the lids, like a sac filled with blood. Under such conditions the patient is unable to completely close the eyes. The cornea retains its normal transparent appearance, but, owing to the elevated conjunctiva about its periphery, appears to be sunken deeply into the eyeball. This condition, together with the dark discoloration of the face and the tumefied features, gives to the patient a peculiarly unnatural expression. A close scrutiny of the skin usually reveals the presence of small abortive

of the countenance frequently enables one to prophesy that the disease will take the confluent form. As the eruption progresses it passes through the usual stages, though somewhat more slowly than in the milder cases. The papules are thickly set, and even at this stage a coalescence of lesions may be noted. The skin is thickened and indurated, and feels like embossed leather. Soon the grayish outlines of the vesicles make their appearance and the confluent aspect of the exanthem becomes accentuated. With the conversion of the vesicular contents into pus, great swelling and œdema develop, particularly about the face and scalp. The eyelids are enormously puffed, and the margin of the upper lid so greatly thickened that it completely overlaps the lower. The nose, lips, and ears are swollen and distorted, imparting to the countenance a most hideous expression. The transformation of the features is so rapid and complete that nurses and physicians who are off duty for a day or two are frequently unable to identify such patients on their return to the wards. The hands and feet are swollen

FIG. 38



Profuse eruption upon hands

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FIG. 39

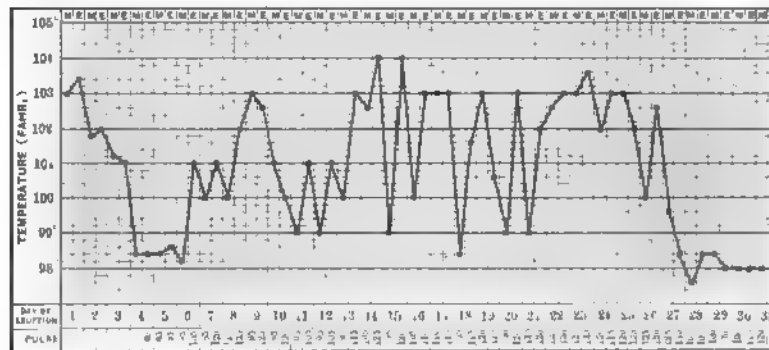


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FIG. 40



W. F. aged thirty-seven years. Case of smallpox in an unvaccinated man, showing the rise of temperature in the initial stage, the secondary or suppurative fever, and a later irregular fever due to abscesses and cellulitis; recovery

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PLATE XXVII.



Extremely Mild Form of Smallpox in an Unvaccinated Child on the Sixth Day of Eruption.
Representing a type of the disease liable to be confounded with chickenpox.

present remarkably mild manifestations of the disease. The exanthem in such cases may amount to merely a half-dozen or a dozen lesions, or in rare instances there may be even a complete absence of the eruption. The mildness of the constitutional symptoms and the paucity of the eruption in these cases may, with reason, be attributed to a certain degree of natural insusceptibility to the disease.

We desire to call attention to the fact that smallpox, under certain circumstances, may depart from its usual life history and, during epidemic prevalence, exhibit in a more or less uniform manner an

FIG. 41



Example of a remarkably mild type of smallpox which has been prevailing for some years in various sections of the United States. Patient unvaccinated.

extraordinary mildness. Such an epidemic has been prevailing in various sections of the United States for the past five or six years. It is said to have been imported into this country from Cuba, where it had existed during the Spanish-Cuban war. From the South this form of smallpox gradually became disseminated throughout the Middle and Western States. The disease was recognized as contagious, as it was seen to spread from one person to another and from town to town. But wherever it appeared it was observed to exhibit the same mild type, rarely resulting in death. On account of its aberrant symptomatology there was considerable diversity of opinion among physicians

as to the nature of this disease. Many regarded it as chickenpox; others contended that it was smallpox. Still others, not being able to reconcile the picture with the symptomatology of either of these two diseases, regarded the new form as *impetigo contagiosa*, or as a cutaneous disease of a new and strange variety.

During the years 1898, 1899, and 1900 there were treated in the hospital under our care 162 patients suffering from this mild type of smallpox. Of this number 138 were unvaccinated, and yet not a single death resulted; 12 of the patients were white and 150 were negroes. (The disease appeared to start among the Southern blacks, but later, in other portions of the country, the whites constituted the great majority of the patients.)

The onset of this type of smallpox does not differ greatly, except in degree, from that commonly seen in the severer forms of the disease. According to information obtained from many of the patients the entire initial illness was often so mild that they were not obliged to remain constantly in bed; some even stated that they had scarcely been ill at all, and yet on close interrogation it was found that all had suffered to some degree from the usual symptoms. In a few patients the initial stage was marked by its usual severity.

The vast majority of patients would not remain in bed after the eruption appeared. They preferred to don their clothes and indulge in various games. It was a novel sight to see these unvaccinated smallpox patients engage in a game of baseball on the eighth or tenth day of the eruption, by which time desiccation was often well advanced. Not more than two or three patients during this epidemic showed symptoms which were at all serious. In some of the mildest cases it was impossible to count as many as a dozen pustules upon the entire cutaneous surface. As a rule, the exanthem was discrete and the lesions sparsely distributed. A few patients, however, exhibited more copious eruptions, even to the extent of producing confluence on the face. In very mild cases the eruption pursued a short, abortive course. Even in the more pronounced cases the duration of the disease was considerably abridged. The course of the disease was identical with that seen in varioloid, and yet in the vast majority of the patients there was no known modifying influence operating such as results from vaccination or a previous attack of the disease.

Why smallpox in the unvaccinated should present itself so generally in such an exceptionally mild form is a problem most difficult to solve. It has been suggested that this form of variola originated in Cuba and that smallpox in the tropics is less severe than in cold climates. We are not sure that this is true, but, even if it were, there is no reason why the disease should not resume its old and familiar form when transferred to temperate or colder regions. It has furthermore been suggested in explanation of the mild type that the modification is due to hereditary vaccinal influence. That this is not true is evidenced by the fact that the disease in the South prevailed largely among negroes, and it is a notorious fact that this race most flagrantly neglects vaccination.

PLATE XXVIII.



An Unvaccinated Negro showing Superficial Confluent Smallpox on the Eighth Day of the Eruption.

PLATE XXIX.



Same Patient as in Plate XXVIII.

Photograph taken 48 hours later indicating the rapidity of the stages of desiccation and decrustation

Indeed, we were able to ascertain by inquiry that the parents of many of our patients had never been vaccinated. Again, a similar mild epidemic occurred in the days of Jenner, before there would have been an opportunity for an hereditary influence to become manifest. Jenner in 1798 wrote:

"About seven years ago a species of smallpox spread through many of the towns and villages of this part of Gloucestershire. It was of so mild a nature that a fatal instance was scarcely ever heard of, and consequently so little dreaded by the lower orders of the community that they scrupled not to hold the same intercourse with each other as if no infectious disease had been present among them. I never saw nor heard of an instance of its being confluent. The most accurate manner, perhaps, in which I can convey an idea of it is, by saying that had fifty individuals been taken promiscuously and infected by exposure to this contagion they would have had as mild and light a disease as if they had been inoculated with variolous matter in the usual way. The harmless manner in which it showed itself could not arise from any peculiarity either in the season or the weather, for I watched its progress upward of a year without perceiving any variation in its general appearance. I consider it, then, as a variety of the smallpox."

Sydenham is said to have described a prototype of the mild variety of smallpox in 1771.

Van Swieten, the great Dutch physician of the eighteenth century, wrote in 1759 as follows:

"The primary fever is often little more than a febricula, and the pustules seldom exceed more than from one to two hundred. The form is so mild that secondary fever is not manifested and constantly is wanting, convalescence coming on on the eighth day of the eruption."

The mildness of the type of smallpox under discussion may be comprehended from the following figures: During the year ending June 30, 1902, there were in the United States 55,857 cases of smallpox with 1852 deaths (a mortality rate of 3.31 per cent.), and in the year previous 38,506 cases and 689 deaths (a mortality rate of 1.79 per cent.). These figures include the smallpox in certain sections of the country where the type was of normal severity.

It is reasonable to presume that in such an epidemic the causative germ of smallpox has become attenuated in its virulency, as a result of certain unknown influences. By no other method of reasoning could we account for the singular and uniform mildness which has characterized this extensive and widespread epidemic. We believe, furthermore, that the infectivity of this mild variety of smallpox is considerably less pronounced than that of classic variola. We have noted that this type of the disease has frequently failed to spread where there appeared abundant opportunity for its diffusion.

Varioloid (Variola Benigna; Variola Modificata; Modified or Mitigated Smallpox).—The term varioloid, from an etymological point of view, would indicate a disease merely bearing a resemblance to variola. The impression thus conveyed is, of course, a false one, for varioloid

is true smallpox in a modified form. This is evident from the fact that the infection arising from this milder form of the disease gives rise to *variola vera* in unprotected persons. Since the introduction of vaccination varioloid has become much more frequent than in former times. Indeed, in well-vaccinated communities modified smallpox is apt to numerically exceed the cases of ordinary *variola*.

It is well known that the immunity conferred by vaccination, although complete at first, becomes in the course of time more or less impaired in the vast majority of individuals. The protective influence from this procedure diminishes very gradually for a variable period of time and may ultimately become entirely extinguished. It is readily comprehensible, therefore, that we may encounter vaccinated persons in whom, on the one hand, there is almost complete protection against smallpox, and, on the other, individuals whose susceptibility to smallpox has quite fully returned. The former, when they contract smallpox, will exhibit the mildest sort of symptoms, with an insignificant eruption, while the latter may develop the most severe confluent or even hemorrhagic *variola*. Between these two extremes one may encounter almost every possible intermediate grade. It should be stated, however, that it is exceptional for the vaccinal protection to be completely lost. Usually a modifying influence upon the course of the disease will be exerted, even when it appears at the outset that the patient is going to suffer from confluent smallpox. The vast majority of vaccinated persons who contract smallpox have the course of the resulting disease favorably influenced.

We class as varioloid all vaccinated cases in which the eruption is markedly abridged in its course and in which there is but little if any secondary rise of temperature. To be sure, cases in which a second attack of smallpox is favorably influenced by an antecedent one would also deserve this designation. We regard as *variola* all unvaccinated cases and all those vaccinated cases in which the eruption pursues its regular course, and is attended with secondary or suppurative fever.

There are certain unprotected individuals who possess more or less natural immunity against smallpox and in whom the disease is mild and of short duration. Some writers would include these cases in the category of varioloid, but we prefer to regard them simply as mild forms of *variola vera*.

We not infrequently meet with cases of smallpox in vaccinated individuals which are so near the dividing line that the determination of the class to which they belong must be postponed until the suppurative stage has passed.

Varioloid cannot always be distinguished in the initial stage from *variola vera*, since the train of symptoms may be the same and of equal severity in each. In many cases, however, the invasive manifestations in varioloid are extremely mild and will warrant a prediction of a sparse exanthem. Unmodified smallpox is so seldom ushered in with mild symptoms that the likelihood of its occurrence after slight constitutional disturbance is remote. It is important to remember, however,

PLATE XXX.

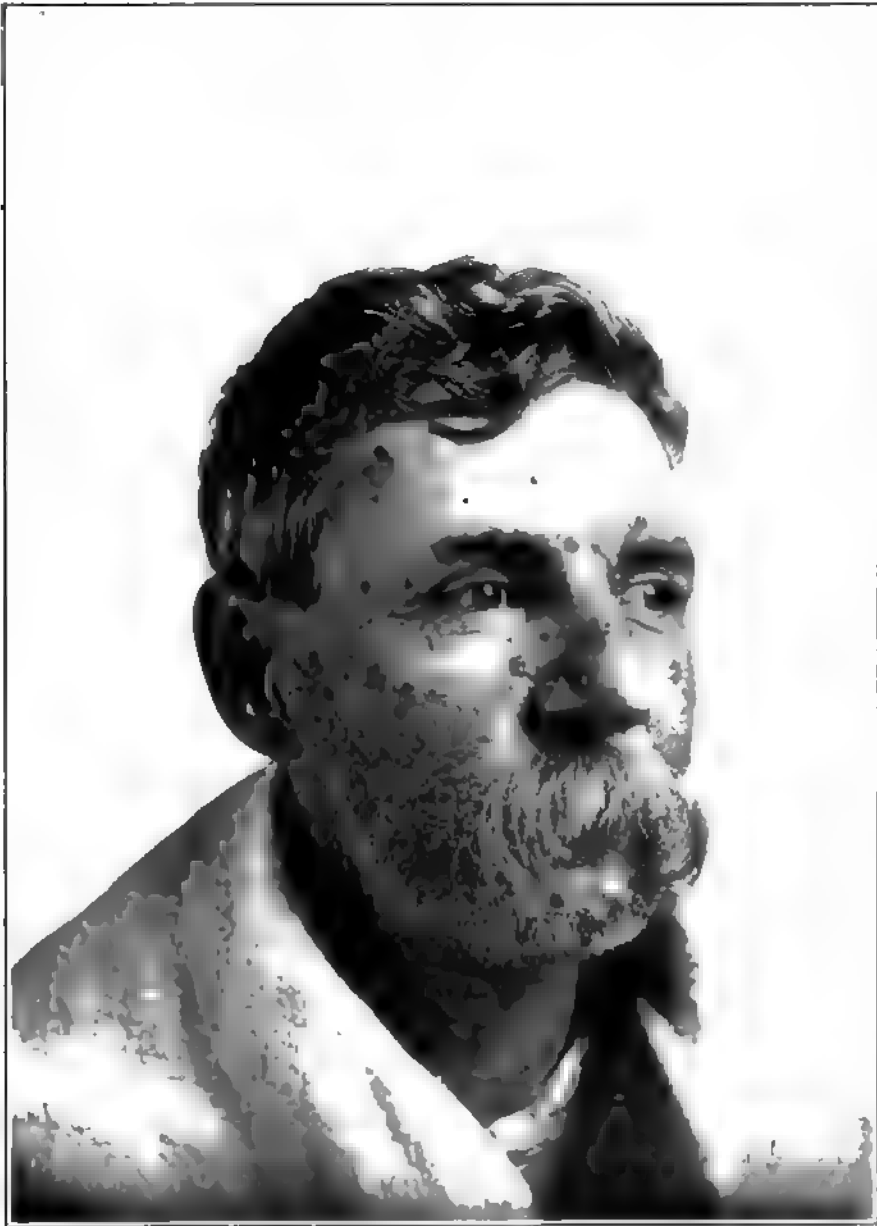


A Remarkably Sparse Eruption of Smallpox in an Unvaccinated Girl.

This patient had obviously but slight susceptibility to the disease. (Rare.)



PLATE XXXI.

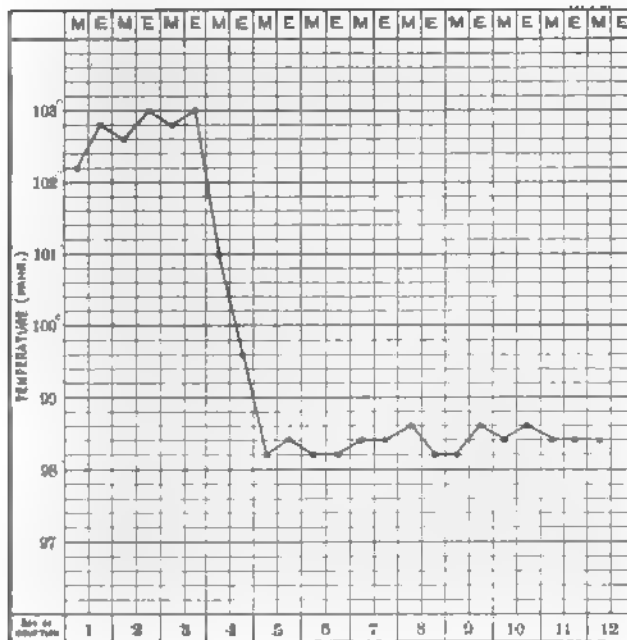


Mild Case of Varioloid in a Man Vaccinated in Infancy.

that a severe initial illness does not preclude the possibility of the development of varioloid.

The duration of the initial stage in varioloid is subject to considerable variation. While this period in variola lasts quite uniformly three days, in varioloid it may be as short as twenty-four to forty-eight hours, or as long as four or five days. At the commencement of the invasive stage the temperature rises to a variable height; upon the outbreak of the eruption it usually drops rather suddenly to the normal or even below this point. Ordinarily no subsequent rise occurs unless complications develop. In other words, the average case of varioloid is attended with

FIG. 42



W. C., aged twenty-nine years. A case of varioloid showing the temperature during the initial stage; the fever began to decline upon the appearance of the eruption.

fever only during the initial stage. With the subsidence of the pyrexia there is a general abatement of all of the systemic symptoms. The headache and backache cease, often with agreeable promptness, and the patient feels quite well again. In every large epidemic of smallpox instances are noted in which artisans and workmen, recovering from the initial stage of a varioloid, resume their daily labors unmindful of the "pimples which have broken out" on them. Mild cases of this character are a fertile source of spread of the disease.

The initial erythematous exantheams, more particularly the morbilliform type, not infrequently develop during the febrile stage of varioloid. Indeed, this prodromal rash, not unlike measles in appearance, is so

commonly followed by an exceedingly sparse eruption that it might almost be regarded when present as the forerunner of varioloid. But if the rash should be petechial or purpuric in character it is, as a rule, an indication that the attack will be severe.

The extent of the eruption varies greatly in different cases of varioloid. The protection may be almost but not quite complete, and the patient may pass through the initial stage but remain free of eruption. To this most benignant form of smallpox the term *variola sine exanthemate*, or *variola sine variolis*, has been given. A case reported by Curschmann well illustrates this type of the disease: "During a severe epidemic of smallpox, a midwife, aged forty years, in the eighth month of pregnancy, fell sick with rigors, followed by violent fever, headache, pain in the back, etc.—apparently the initial stage of smallpox. On the fourth day, however, she was free from fever, and, in spite of the most careful examination, exhibited no trace of the expected eruption. Ten days after the commencement of the disease, feeling at this time perfectly well, she gave birth to a child covered with a smallpox eruption, evidently just appearing, which developed still further and in three days terminated in death during the stage of suppuration."

There is nothing peculiar about the eruption of varioloid except that it is milder in its course, of shorter duration than that of variola, and exhibits various irregularities. It almost always appears on the face and rapidly spreads to other parts of the body, although at times it makes its appearance on the trunk and extremities quite as early as on the face. The lesions do not develop quite as regularly as in unmodified smallpox, it being not unusual to find some pustules larger and farther advanced than others. The eruption may be limited to a very few lesions on the face and hands, or it may assume a semiconfluent form, and also invade other parts of the body to a considerable extent. We have observed several undoubted cases in which but a single lesion could be found upon the entire cutaneous surface. In the milder forms the lesions do not pass through all the stages, but become abortive and dry up at an early period. In the severer forms the eruption, although confluent or semiconfluent, pursues a distinctly modified course. In such cases the lesions do not penetrate into the deeper layers of the skin, but remain limited to the epidermis. Hence the course of eruption is shorter, the process of suppuration is abridged, and the lesions desiccate early; in addition the crusts are rapidly thrown off and there is little or no scarring. This variety of smallpox was called by the earlier writers "confluent superficial." We have seen vaccinated patients with confluent eruptions which in the beginning looked most formidable and dangerous; but the magic influence of the vaccine disease was fortunately there to convert the serious malady into a comparatively trifling affection.

More frequently the eruption of varioloid is discrete and sparse, but runs the same mild course. The papules are very early converted into vesicles, and reach the pustular stage on the third or fourth day, completing their evolution from the fifth to the seventh day, when desiccation

PLATE XXXII.

Fig. 1.



Fig. 2.



Series of Photographs showing a Modified Smallpox after an Infantile Vaccination in a Girl Fifteen Years of Age. Recovery without any pitting.

PLATE XXXIII

FIG. 3



FIG. 4



Same Patient as seen in Plate XXXII.

Lesions are seen to dry up rapidly and to effect no destruction of the true skin



PLATE XXXIV.



Tuberculated Elevations (*Variola Verrucosa*) left after
the Shedding of the Crusts.

begins. The pustules are frequently acuminate or conical, quite unlike the large, hemispherical pustules seen in unmodified smallpox. They dry up quickly, forming thin, brownish crusts, which fall off much sooner than in the ordinary form of the disease. After decrustation reddish stains, later becoming brown, may be left, but these are not as persistent as in *variola vera*. Owing to the superficial character of the skin involvement in varioloid, most of the patients escape without any permanent scarring.

When the modification of the eruption is still greater, it is not unusual to find that the lesions develop into large, solid, conical papules, having at their apices small vesicles which rapidly desiccate and form thin crusts. After the crusts have fallen off the lesions remain tuberculated for some time. Viewing a patient with this condition from a little distance it is often difficult to say whether the eruption is just beginning or terminating. Sometimes these tubercles present the appearance of warty excrescences; to this form of the eruption the name *variola verrucosa*, or *wart pox*, has been given. This modification of the smallpox eruption is seen usually upon the face. In the course of time the elevations flatten down and disappear, as a rule, without leaving scars. Another somewhat common form of the eruption is that known as *variola miliaris*; in this variety the majority of the vesicles are very small, not larger than millet seeds; without progressing further they turn yellow, desiccate and disappear. Not rarely a few tolerably well developed pustules are found mixed with these smaller lesions.

Variola corymbosa is a designation applied to those eruptions which exhibit grouping of rather flat pustules in the form of corymbs or clusters. It is alleged by some writers that the mortality rate is particularly high in cases showing this character of eruption.

The contents of abortive vesicles and pustules frequently desiccate without rupturing, producing hard, horny, convex, shining, reddish-brown crusts. This form is designated *variola cornea*, or *horn pox*. The reddish-brown, horny crusts are quite characteristic of smallpox. They are particularly common in varioloid, and often materially aid one in the diagnosis of doubtful cases. They are of distinct value in cases which are seen for the first time at a late stage, when the original appearance of the eruption is altered. The horny crusts are seen most frequently on the hands and forearms, but may also be noticed at times on the face.

In the form of the eruption termed *variola siliquosa*, there is a retrogression of the pustules with absorption of the contents and the production of epidermal cavities filled with air. In addition to the above irregular forms of the smallpox eruption, writers have described other varieties, such as *variola conica*, *crystallina*, *emphysematica*, *fimbriata*, *lymphatica*, *pemphigosa*, *pustularis*, *rosea*, *morbillosa*, *carbunculosa*, *globulosa*, etc.

These various designations do not indicate separate varieties of the disease, but merely different appearances produced by more or less trifling changes in the lesions.

The mucous membrane of the mouth and upper air passages is usually affected in varioloid, but much less severely than in unmodified smallpox. The various complications involving the skin, eye, and other organs may occur in varioloid, although they are decidedly less frequent and less severe in this form of the disease. In rare instances grave affections of the brain and spinal cord may complicate mild cases of smallpox; to this more extended reference will be made in considering the complications of variola.

Inoculated Smallpox.—Although the practice of inoculation of smallpox is completely obsolete and prohibited in most countries by statutory legislation at the present time, it is of interest to know the clinical appearances produced by it. Not having had any practical experience with this form of the disease, we prefer to present the description given by Gregory:

“Inoculation is performed by introducing into the arm at the insertion of the deltoid, by means of a lancet, a minute portion of variolous matter. The thin lymph of a fifth-day vesicle is to be preferred to the well-concocted purulent matter of the eighth-day matter, but both are efficient. One incision only is to be made. A minute orange-colored spot is perceptible, by aid of the microscope, on the second day; on the third or fourth day a sensation of pricking is observed in the part. The punctured point is hard, and a minute vesicle, whose centre is depressed, may be observed surmounting an inflamed base. On the fifth day the vesicle is well developed and the areola commences. On the sixth day the patient feels stiffness in the axilla, with pain. The inoculated part has become a hard and inflamed phlegmon. The subjacent cellular membrane has become involved in the inflammatory action. On the evening of the seventh day or early on the eighth day, rigors, headache, a fit of syncope, vomiting, an offensive state of the breath, alternate heats and chills, languor, lassitude, or in the child an epileptic paroxysm, announce the setting in of fever. The constitution has taken alarm and sympathizes with the progress of the local disorder.

“On the appearance of the febrile symptoms the inflammation of the arm spreads rapidly. An areola of irregular shape is soon completed, which displays within it minute confluent vesicles. On the tenth day the arm is hard, tense, shining, and very red. The pustules discharge copiously and ulceration has evidently penetrated the whole depth of the corium.

“On the eighth day spots of variolous eruption show themselves in various and often most distant parts of the body. In a very large proportion of cases the eruption is distinct and moderate. Two hundred vesicles are counted a full crop. Sometimes not more than two or three papulæ can be discovered, which perhaps shrivel and dry up without going through the regular process of maturation. At other times the eruption is full and semiconfluent, passing through all of the stages of maturation, scabbing, and cicatrization. Between these extremes every possible variety may be observed. The truly confluent

eruption with affection of the mucous membrane is rare. Secondary fever, therefore, is not common, at least in any intensity.

“The rules laid down for the safe conduct of inoculation were principally the following: It should be performed exclusively in persons free from actual bodily disease, and neither plethoric nor scrofulous. It may be safely practised at all ages, beginning at the third month. It is improper to inoculate during pregnancy, on account of danger to the child *in utero*. Laxative medicine, a moderate diet, abstinence from all fermented and spirituous liquors, cool chambers, gentle exercise in the open air, light clothing—all contribute in their several degrees to the successful result.

“The influence of inoculation in lessening the mortality of smallpox was something quite extraordinary and scarcely credible. With ordinary precaution in the choice and preparation of subjects, not more than 1 in 500 cases will terminate unfavorably. Had not the discovery of Jenner interfered to interrupt its extension and improvement, inoculation would have continued to this day, increasing yearly in popularity. It cannot be doubted that improvements in medical science generally would have shed additional lustre on this practice.”

By no means all of the older writers were so favorably disposed toward inoculation as Gregory. Considerable diversity of opinion existed as to the mortality rate after this procedure. Dr. Jurin, after examining the London bills of mortality for forty-two years, concluded that 1 among every 50 persons inoculated died. Apart from the danger to the individual, great disadvantage arose from the continuance of the disease by inoculation and the establishment of numerous foci of contagion from which smallpox could be spontaneously disseminated. It is alleged that the annual mortality from this disease was increased by the practice of this procedure.

Smallpox in the Pregnant Woman.—The functions of the uterus are disturbed with striking frequency during the course of smallpox. The menses quite uniformly appear out of their normal course, and in pregnant women abortion or premature birth is an accident of common occurrence, and one that adds greatly to the danger of the disease. Although the premature advent of menstruation and even the occurrence of abortion are not uncommon events in many other infectious diseases, their occurrence in smallpox is so extremely frequent as to suggest a direct relationship with the variolous process. It is probable that abortion is the result of the uterine hemorrhage which is so commonly excited during an attack of smallpox. In some cases it may be due to the death of the foetus which is suffering from an intrauterine variola.

The symptomatology and course of smallpox are often markedly influenced by the pregnant state. The gravity of the disease is considerably augmented as a result of the coexistence of this condition. Of 113 cases of smallpox in pregnant women treated under our care, 35 died, constituting a mortality rate of about 31 per cent. In unvaccinated women the death rate has been truly frightful, twenty dying out of a total of twenty-seven such cases, giving a mortality rate of

over 74 per cent. Of 85 women vaccinated at some previous remote period, 14 died, the mortality rate being about 16 per cent.

		Died.	Mort. rate.
Smallpox in pregnant women (vaccinated)	85	14	16 %
" " " (unvaccinated)	27	20	74 %
" " " (vaccine condition unknown)	1	1	
Total	113	35	30 %

If abortion occurs during the initial stage the disease is apt to assume the form of purpura variolosa, in which case death is practically inevitable. Not every case in which abortion or premature birth occurs in the earlier stages of the disease takes on this malignant form. In attacks which are considerably modified by previous vaccination, the smallpox process is, of course, not so seriously affected by the occurrence of this accident. Even in cases of true variola, when the loss of blood is not very great—which is rarely the case—the variolous process may pursue its regular course and progress to a favorable termination. In but 5 cases out of 31 did recovery occur, when abortion took place before the tenth day of the eruption.

For facts in support of what has been said relative to smallpox exciting abortion when the pregnant are attacked, and to the increased mortality from the disease when this complication arises, the reader is referred to the appended table.

On examination of the table it will be seen that out of 113 cases of smallpox, including both variola and varioloid, occurring in pregnant women, 65, or 58.4 per cent., suffered from abortion or premature delivery. Of the remaining 48, 8 died without aborting, 9 recovered without abortion occurring and were delivered at term, and 31 were discharged still carrying the foetus, but were not heard from after leaving the hospital. Of the 65 cases (including variola and varioloid) in which abortion or premature birth occurred, 26, or 40 per cent., died.

Abortion occurs in variola more frequently than in varioloid, though the difference is not as pronounced as one might expect. The table shows that of our 49 cases of variola, 35, or 71.42 per cent., miscarried, and out of 63 cases of varioloid, 31, or 49.2 per cent., miscarried. It is probable that some of the patients who left the hospital carrying the foetus aborted before the completion of the period of gestation, for we have observed this to occur not infrequently.

When miscarriage occurs in variola it proves, of course, a much more serious complication than when it occurs in varioloid. By reference to the table we find, out of 35 cases of variola thus complicated, 26, or 74.28 per cent., died; while among 31 cases of varioloid in which the complication occurred but 1 died, and this death resulted from puerperal peritonitis.

The period at which miscarriage most frequently takes place is during the second, or eruptive stage of the disease. It not only occurs during the course of the disease, but frequently during convalescence, and in many instances even several weeks after complete restoration to health. Miscarriages prove the more serious the earlier they occur in the

course of smallpox. This is shown in the accompanying table, which includes cases of variola and varioloid:

**DAY OF THE ERUPTION ON WHICH MISCARRIAGE OCCURRED, WITH
CORRESPONDING MORTALITY.**

	Cases.	Deaths.
Initial stage	4	2
On or before the fifth day of eruption	30	17
From fifth to twentieth day	16	8
Subsequent to twentieth day	14	0

Miscarriage occurs doubtless much more often during the initial stage of the disease, particularly during epidemics, than the table would lead us to believe. In such cases death usually follows so speedily that the true nature of the disease is often overlooked, or, if recognized, the critical condition of the patient forbids removal to the hospital; hence the table shows a relatively small number of miscarriages occurring at this stage of the disease.

The gravity of smallpox in pregnant women appears to vary considerably in different epidemics. We have had the opportunity of observing these cases in three rather extensive periods of smallpox prevalence. The following table will indicate the comparative mortality rates of pregnancy and abortion complicating smallpox during the three epidemics:

	Number.	Deaths.
1871-72. Pregnancies	46	14 or 30.43 %
Abortions and premature births	27	10 or 37.00 "
Variola	10	10 or 100 "
Varioloid	13
1881-82. Pregnancies	31	16 or 51.61 %
Abortions and premature births	19	13 or 68.42 "
Variola	15	13 or 86.66 "
Varioloid	4	1 or 25.00 "
1901-02. Pregnancies	36	5 or 13.88 "
Abortions and premature births	20	3 or 15.00 "
Variola	6	3 or 50.00 "
Varioloid	14

The above tables show that the mortality rate in pregnant smallpox women in 1871-72 was 30.43 per cent.; in 1881-82, 51.61 per cent., and in 1901-02, 13.8 per cent. Of those that aborted the mortality rate in 1871-72 was 37 per cent.; in 1881-82, 68.42 per cent., and in 1901-02 only 15 per cent.¹

¹ Since compiling the above figures, eight pregnant women with smallpox have been admitted to the hospital. Of this number five aborted, one of whom died.

SMALLPOX IN PREGNANT WOMEN.

No.	Age	Character of disease.	Whether vaccinated, and if so, character of cicatrix.	Month of pregnancy when attacked.	Stage of disease at which abortion occurred.	Result.	Remarks.
1	26	Varicella (confluent).	Poor scar.	4	Recovered.	Delivered at term; child healthy; was successfully vaccinated.
2	27	Varicella.	Good "	2	8th day of eruption.	Died 5th day of eruption.	
3	25	Varicelloid.	Fair "	3	18th day of eruption.	Recovered.	
4	21	Varicella.	Poor "	2	3d week.	"	
5	22	Varicelloid (mild).	10 poor scars.	5	After leaving hospital.	"	Ran away from hospital, and subsequently aborted.
6	24	Varicella (confluent).	1 fair scar.	8	1st day of initial fever.	Died 2d day of eruption.	
7	20	Varicella.	1 poor "	5½	Recovered.	Delivered at term.
8	25	Varicelloid.	1 fair "	3	5 weeks after leaving hosp.	"	
9	22	Varicella.	Not vaccinated	7½	1st day of eruption.	Died 6th day of eruption.	
10	26	Varicelloid.	1 poor scar.	3	Recovered.	Delivered at term.
11	16	Varicella.	Not vaccinated	3	Died 9th day.	Patient said to have been pregnant, but abortion did not occur.
12	28	Varicelloid.	Good scar.	2	10 days after leaving hosp.	Recovered.	
13	23	"	" "	6½	25th day of eruption.	"	The fetus presented a few red spots evidently the result of a slight vesicular eruption.
14	18	Varicelloid (mild).	" "	8½	9th day of eruption.	"	
15	21	Varicelloid.	Poor "	2	"	
16	29	"	" "	5	Died 5th day of eruption.	
17	■	Varicelloid (mild).	Good "	9	Delivered at early stage of eruption.	Recovered.	
18	30	Varicella.	Poor "	5½	2d day of eruption.	Died 3d day of eruption.	
19	27	Varicelloid.	Fair "	7	Recovered.	
20	27	Varicella.	Poor "	3	1st day of eruption.	Died 7th day of eruption.	
21	25	Varicella (confluent).	Not vaccinated	7 or 8	3d day of eruption.	Died 11th d'y of eruption.	Child lived one or two days; died of debility.
22	32	Varicelloid.	4 good scars.	8	Recovered.	Delivered at term.
23	20	Varicella.	Not vaccinated	6	Died 7th day of eruption.	Died while in the act of abortion.
24	17	Varicella (confluent).	" "	4	6 weeks after leaving hosp.	Recovered.	Aborted six weeks after leaving hospital.
25	24	Varicella.	Fair scar.	3	Died 27th d'y of eruption.	Died of pleurisy, without aborting.
26	19	Varicelloid (mild).	5 good scars.	6	1 month after leaving hosp.	Recovered.	Aborted one month after leaving hospital.
27	26	Varicella.	Fair scar.	5	3d day of eruption.	Died 6th day of eruption.	
28	22	Varicelloid (mild).	Poor "	2	2d day of eruption.	Recovered.	
29	30	Varicella.	3 poor scars.	5½	4th day of eruption.	"	
30	20	Varicelloid	Fair scar.	3	1st day of eruption.	"	Infant died of debility.
31	25	Varicella.	Good "	5½	"	Delivered at term.
32	25	Varicella (confluent).	6 poor scars.	4	5th day of eruption.	"	
33	45	Varicelloid (mild).	Fair scar.	6	"	
34	19	Varicelloid	Poor "	6	"	Delivered at term.

No.	Age	Character of disease.	Whether vaccinated, and if so, character of cicatrix.	Month of pregnancy when attacked.	Stage of disease at which abortion occurred.	Result.	Remarks.
35	26	Variola.	Not vaccinated	7½	1st day of eruption.	Died 4th day of erup.	
36	18	Varioloid.	3 fair scars.	3½		Recovered.	
37	26	Variola.	Unknown.	8	Early stage of eruption.	Died.	Died on way to hospital; infant died of debility.
38	41	Varioloid.	2 good scars.	8	3d day of eruption.	Recovered.	Infant died of debility.
39	28	"	Fair scar.	4½		"	Delivered at term; child successfully vaccinated.
40	30	"	2 fair scars.	6		"	Delivered at term; child successfully vaccinated.
41	25	"	Good scar.	3	1st day of eruption.	"	
42	20	Variola.	Poor "	6½	5th day of eruption.	Died 8th day of erup.	Infant lived about 24 hours.
43	22	Varioloid.	Good "	6		Recovered.	Delivered at term; child died when two months old, without being vaccinated.
44	28	"	4 good scars.	6		"	Delivered at term; child successfully vaccinated.
45	21	"	8 " "	5	During maturation.	"	
46	25	Varioloid (mild).	3 fair "	6		"	
47	21	Variola (confluent).	Not vaccinated	8½		"	
48	32	Variola.	1 poor mark.	5	Aborted 12th day of eruption.	Died.	
49	30	Varioloid	1 " "	8	Aborted 2d day of eruption.	Recovered.	Child successfully vaccinated; died later of debility.
50	34	Variola.	Not vaccinated	5	Died without aborting, 6th day of eruption.	Died.	
51	26	Varioloid.	3 fair scars.		Aborted 3d day of eruption.	"	Died of puerperal peritonitis.
52	18	"	1 good scar.	7	Discharged carrying fetus.	Recovered.	
53	29	"	6 fair and 2 poor scars.	3	25th day of eruption.	"	
54	22	"	2 good scars.	2	Discharged carrying fetus.	"	Delivered at term.
55	22	Variola (hemorrhagic).	Not vaccinated	6 weeks	Aborted before death.	Died.	
56	25	Varioloid.	2 good scars.	6	Discharged carrying fetus.	Recovered.	
57	36	Variola (hemorrhagic).	1 poor scar.	7	1st day of eruption.	Died 7th day of erup.	
58	40	Varioloid (mild).	2 poor scars.	6	Discharged carrying fetus.	Recovered.	
59	38	Varioloid.	1 fair scar	2	Discharged carrying fetus.	"	
60	19	Variola.	Not vaccinated	7	Aborted before death, 7th day.	Died.	
61	22	"	" "	5	Day before eruption.	Died 6th day of erup.	
62	33	Varioloid.	2 good scars.	7	Discharged carrying fetus.	Recovered.	
63	23	Variola (confluent).	Not vaccinated	5	Aborted 16th day of eruption.	Died 15th dy	
64	19	Variola (confluent).	" "	3	Aborted 11th day of eruption.	Died 11th dy.	
65	18	Variola (confluent).	" "	3	Discharged carrying fetus.	Recovered	Aborted later.
66	36	Varioloid (mild).	2 good and 2 fair scars.	6	Discharged carrying fetus.	"	
67	29	Varioloid.	1 good scar.	6½	Aborted before eruption.	"	
68	24	Variola (confluent).	Not vaccinated	3	Aborted 11th day of eruption.	Died 11th dy.	
69	"	Variola (confluent).	" "	8	Aborted 1st day of eruption.	Died.	Infant successfully vaccinated; developed 14 papules, died of debility.
70	24	Variola (hemorrhagic).	" "	4	Aborted 8th day of eruption.	Died.	

No.	Age	Character of disease.	Whether vaccinated, and if so, character of cicatrix.	Month of pregnancy when attacked.	Stage of disease at which abortion occurred.	Result.	Remarks.
71	23	Varicellid.	-----	5½	Discharged carrying fetus.	Recovered.	
72	27	Varicella.	1 fair scar.	4	Aborted 19th day of eruption.	"	Fetus had well-marked varicellous vesicles scattered over body.
73	30	Varicella (hemorrhagic).	1 " "	5	Died 7th day without abort.	Died.	
74	30	Varicella.	2 poor scars.	5	Aborted 7th day of eruption.	Died 7th day.	
75	19	"	Not vaccinated	1	Aborted 1st day of eruption.	Died 1st day.	
76	30	Varicellid.	2 good scars.	3	Discharged carrying fetus.	Recovered.	
77	28	Varicella (confluent).	Not vaccinated	4	Aborted 8th day of eruption.	Died 8th day.	
78	25	Varicella (hemorrhagic).	1 poor scar.	5½	Aborted 1st day of eruption.	Died 4th day.	Infant infected in utero, exhibiting eruption on 9th day of life; died on 14th day.
79	25	Varicella (confluent).	Not vaccinated	5½	Died without aborting.	Died 8th day.	Cæsarean section performed immediately after death, but infant found dead.
80	17	Varicella (semiconfluent).	" "	5	Discharged carrying fetus.	Recovered.	Delivered at term.
81	18	Varicellid (mild).	1 good scar.	7½	Aborted 6th day of eruption.	"	Infant vaccinated at birth; vaccination took; later contracted varicellid and died.
82	27	Varicellid.	2 poor scars.	3	Aborted 4th day of eruption.	"	
83	27	"	1 fair mark.	4½	Aborted 23d day of eruption.	"	
84	35	"	1 fair scar.	5½	Discharged carrying fetus.	"	Delivered at term.
85	21	Varicella (hemorrhagic).	Not vaccinated	5½	Died without aborting.	Died.	Post-mortem Cæsarean section; fetus dead.
86	21	Varicellid.	1 fair scar.	3	Delivered 21st day of eruption.	Recovered.	Child vaccinated three times, but without success remained well.
87	23	"	2 good scars.	3	Aborted 1st day of eruption.	"	Child was successfully vaccinated, but soon developed smallpox eruption and died; infection in utero.
88	29	Varicella (confluent).	Not vaccinated	7	Discharged carrying fetus.	"	Delivered at term.
89	32	Varicellid.	Vac. 10 days before erup.	8	Aborted 17th day of eruption.	"	
90	30	"	Vaccinated before eruption.	2	Aborted 18th day of eruption.	"	
91	24	"	1 fair scar.	7	Discharged carrying fetus.	"	Delivered at term.
92	18	Varicella (confluent).	Not vaccinated	5	Discharged carrying fetus.	"	Delivered at term.
93	27	Varicellid.	Vaccinated before eruption.	7	Aborted 23d day of eruption.	"	Child at birth was dead and covered with a discrete smallpox in the pustular stage.
94	25	"	1 good and 1 poor scar.	9	Delivered 2 days before eruption.	"	Baby vaccinated, but without success; developed smallpox eruption and died.
95	25	"	2 good scars.	7	Discharged carrying fetus.	"	Delivered at term.
96	28	Varicella (confluent).	Not vaccinated	5	Aborted just before death 3d day.	Died.	
97	30	Varicellid.	1 good scar.	4	Discharged carrying fetus.	Recovered.	
98	24	Varicella (confluent).	Not vaccinated	9	Delivered on 9th day.	"	Child was successfully vaccinated; smallpox appeared on 7th day, and child died; infection in utero.
99	28	Varicellid.	1 fair scar.	6	Discharged carrying fetus.	"	Delivered at term.
100	39	"	1 poor "	8	Discharged carrying fetus.	"	Delivered at term.

No.	Age	Character of disease.	Whether vaccinated, and if so, character of cicatrix.	Month of pregn'cy when attacked.	Stage of disease at which abortion occurred.	Result.	Remarks.
101	23	Variola.	Not vaccinated	8½	Aborted 1st day of eruption.	Recovered.	
102	23	"	1 poor scar.	8	Aborted 9th day of eruption.	"	Child at birth healthy; successfully vaccinated; 12 days later a half-dozen smallpox papules appeared; child died of erysipelas.
103	21	Varioloid.	1 fair "	8	Delivered 1st day of eruption.	"	Smallpox eruption appeared on child 10 days after birth; infection in utero.
104	24	"	1 good "	4	Discharged carrying foetus.	"	Delivered at term.
105	23	"	2 good scars.	8	Discharged carrying foetus.	"	
106	42	Variola.	1 fair scar.	2½	Discharged carrying foetus.	"	
107	26	Varioloid.	2 poor scars.	9	Delivered at term	"	
108	29	"	1 fair scar.	4	Aborted 37th day of eruption.	"	Foetus showed a sparse vesicular eruption.
109	25	"	2 good scars.	6	Discharged carrying foetus.	"	
110	35	"	2 fair "	6	Aborted 28th day of eruption.	"	
111	32	"	2 good "	6	Aborted 1st day of eruption.	"	
112	22	Variola (hemorrhagic).	Not vaccinated	6	Aborted 5th day of eruption.	Died 5th day.	
113	27	Varioloid (mild).	Vaccinated 16 days before eruption.	2	Discharged carrying foetus.	Recovered.	

Smallpox in the Fœtus.—During an attack of smallpox the causative germ, in all probability, circulates in the blood stream of the patient. Therefore, when a pregnant woman suffers from variola, we would naturally expect the fœtus to be likewise attacked and to pass through all of the phases of the disease simultaneously with the mother. Strange to say, however, this is but seldom the case. In a minority of instances the fœtus does become infected, but not synchronously with the infection of the mother. Indeed, in most cases in which the fœtus develops smallpox it passes through a period of incubation in the same manner as if it were in the outer world; that is to say, about two weeks elapse from the time the mother shows symptoms until the disease appears in the child. From this observation, which is quite generally the experience of most writers, it would seem that the infant *in utero* ordinarily becomes infected, not through the maternal circulation, but through contact or proximity. If the blood of the mother were the infecting medium the disease in the fœtus should be of constant occurrence. There are rare cases in which the fœtus contracts smallpox after an exposure to the disease by a mother who happens to be an immune. In such cases it is difficult to understand how the causative agent could reach the infant *in utero* save through the maternal blood.

Smallpox may be communicated to the fœtus *in utero* at any time between the fourth month of gestation or possibly earlier and the full term. When infection takes place in the earlier stages of intrauterine life, the fœtus usually perishes and is expelled in three or four days, or it may be retained for three or four weeks after life has become

extinct. There are well-authenticated instances in which the child suffers and recovers from an intrauterine attack of smallpox, and is born at term with variolous scars.

When the infection takes place during the later periods of pregnancy the child at birth may be covered with the eruption, which may represent any stage of development. This occurrence is so well authenticated that it is unnecessary to quote any cases from literature. We have ourselves met with four or five instances of this character. In one case a six months' foetus presented a few red spots which evidently resulted from a mild vesicular eruption. In another instance an infant was born at the eighth month, on whose body at birth the eruption

FIG. 43



Smallpox contracted *in utero* and appearing nine days after birth; the vaccine lesion seen upon the arm resulted from vaccination on the second day after birth.

was just appearing. In a third case a four months' foetus was expelled on the thirty-seventh day of the maternal eruption. The eruption on the child was rather sparse, consisting of two whitish, variolous pocks on the sole of the right foot, one on the heel of the left foot, one on the chest, one on the back, and two firm lesions upon the palm of each hand.

The fourth case occurred in a colored child (Fig. 44) born at eight months, on the thirty-third day of the mother's eruption, the latter suffering only from a very mild varioloid. The infant had evidently been dead for some days, as the epidermis was detached from the underlying corium in large areas. Smallpox lesions in the pustular stage (about fifth or sixth day) were present upon the face, extremities, and body, but not profusely. It was calculated that the exanthem in the

child began about twenty-seven days after the eruption appeared in the mother.

The child of a variolous mother may be infected with smallpox *in utero* and be born free of lesions, the eruption appearing some days after birth. If the infant is infected during parturition the outbreak of the eruption may be delayed for a fortnight after it has entered the

FIG. 44



Colored child, born dead at term, with the smallpox eruption present in the stage of pustulation, the mother at the time convalescing from the disease.

world. If it is infected earlier the eruption may appear on the first, second, or third day of life, or at any period within two weeks. We have observed this phenomenon on numerous occasions. Fig. 43 represents a child born on the first day of the mother's eruption, which was hemorrhagic and rapidly fatal. The infant developed the eruption on the ninth day of its life and succumbed to the disease on the fourteenth day. It was vaccinated on the second day, on admission to the hospital, and although the vaccination took it was not sufficiently advanced to materially modify the smallpox exanthem.

The frequency of fetal infection does not seem to bear a relationship to the severity of the disease in the mother. Pregnant women suffering from the severest form of confluent variola do not communicate the disease to the foetus more often than those who have the disease in the mildest possible form. Indeed, as already suggested, infection of the foetus may take place through the mother, although she personally remains free of the disease. A number of curious cases of this nature have been reported. Jenner¹ records two cases which came under his observation; one of the cases is detailed by him as follows:

"A few days previous to her confinement (Mrs. W.) she met with a very disgusting object, whose face was covered with smallpox. The smell and appearance of the poor creature affected her much at the time, and though she mentioned the circumstance on her return home she had no idea that her infant could suffer from it, having had smallpox herself when she was a child. During a few days after its birth the little one seemed quite well, but on the fifth day it became indisposed and on the seventh day the smallpox appeared. Mrs. W. was not sensible to any indisposition herself from this exposure, nor had she any appearance of the smallpox." Other cases of the same character might readily be quoted from literature.

When a pregnant woman undergoes smallpox without miscarriage occurring, the susceptibility to the disease is not destroyed in the infant, except in rare cases. Susceptibility to the vaccine disease, in the vast majority of instances, is, we think, evidence of susceptibility to smallpox. Now and then an infant is born under the circumstances named that will not respond to vaccinia. We have met with three or four such cases. A woman suffering from a well-marked varioloid gave birth in the hospital to a child at term, on the twenty-first day after the appearance of the maternal eruption. The child was vaccinated with glycerinated lymph on three successive occasions, but without success. It remained in the hospital for three weeks and continued perfectly well. In another instance a woman suffering from mild varioloid gave birth to a child at term during the initial stage of the disease. The infant was vaccinated on successive occasions after admission to the hospital, but without securing a "take." A profuse smallpox eruption appeared upon the child on the seventeenth day of its life, which proved fatal.

Concerning the occasional failure of the offspring of variolous mothers to respond to vaccination, it may be said that it is sometimes very difficult, under ordinary conditions, to successfully vaccinate very young infants. In such cases a successful result may sometimes be obtained at a later period—say, at the age of four or five months. This was exemplified in a case reported by Rigden, in which a mother with varioloid gave birth to an infant at term during the height of her eruption. She made a good recovery and was able to nurse her child almost from the day of its birth. The infant was vaccinated the day after its birth, but

¹ Medico-Chirurgical Transactions, vol. i. p. 274.

without success. Between the age of four and five months another attempt was made, with a successful result.

It is of interest to note that in the case just quoted and in our first case the child in each instance was insusceptible at birth to both vaccinia and smallpox. The failure to secure a successful vaccination in our second case may possibly be attributed to the use of inert virus.

But in the vast majority of instances smallpox in the pregnant woman does not destroy the susceptibility to vaccinia in the infant. Our own experience and that of other writers constitute adequate proof of this statement. Rigden¹ reports six cases of successful vaccination in infants born of mothers suffering from smallpox. In these cases vaccination was performed between the ages of three and six months, and was uniformly successful. We have in a score or more of instances successfully vaccinated children who were born of variolous mothers; some of these infants were vaccinated as soon as they were born, while others were only successfully vaccinated several months later. A picture of a successful result of a vaccination at birth is shown in photograph. (Fig. 1 in the chapter on Vaccinia.)

When the infection has occurred *in utero*, vaccination of the infant at birth frequently mitigates the character of the subsequent eruption. If a week or more elapses between the time of vaccination and the development of the variolous exanthem, the lesions are apt to be modified. When the eruption develops within the first week after birth, little or no modification is to be expected.

We must dissent from the view expressed by Roger² that smallpox in the newborn infant differs clinically in any essential manner from variola in the adult. Roger contends that infants born of variolous mothers usually present a more or less latent smallpox, characterized by hypothermia, with or without a slight eruption which commonly comes out in crops and aborts in the papular stage. There is also a tendency to icterus; a fatal termination occurs in most cases. Roger says: "At first sight the newborn appeared well constituted; their general condition was good, and nothing could have caused a congenital infection to be suspected if one had not taken their temperature. All of the infants were hypothermic. . . . In six infants death occurred without their presenting any symptoms suggesting variola in any way." We have on a number of occasions seen newborn infants develop severe and even confluent smallpox. We are not familiar with a congenital variola which may exist without an eruption or be characterized by a sparse exanthem which is arrested in the papular stage. That most infants born of variolous mothers are not really suffering from smallpox at birth is proved by the fact that they will, in the vast majority of cases, respond to vaccination.

¹ British Medical Journal, February 24, 1877.

² Les Maladies Infectieuses, Paris, 1902.

THE URINE IN SMALLPOX.

That excellent French physician and teacher, Trousseau, early observed that albumin was frequently found in the urine in smallpox. He says: "Albuminuria is almost as common in confluent smallpox as in scarlet fever. There is this difference, however, that in scarlatina the albuminuria appears during the decline of the disease, and in confluent smallpox during the acute period of the disease. Extensive observations by Abeille have shown that in confluent smallpox, as in scarlatina, albuminuria is met with in about one-third of the cases."

Our own observations are based upon 1088 urinary examinations in 128 cases of smallpox. The specific gravity was determined in the ordinary manner with the urinometer; 524 examinations gave an average specific gravity of 1018. The presence of indican and the amount thereof both exhibited marked variability. Some cases of severe variola showed a considerable amount of indican, while in others it was absent. The diurnal fluctuations in amount were striking; it was not uncommon to find an abundance one day, and twenty-four hours later to note its absence.

In selecting the subjects whose urine was to be examined, patients with very mild varioloid who were scarcely ill were excluded. The urine was repeatedly examined in 83 patients suffering from variola and in 26 patients with varioloid. Of 83 cases of variola, 66½ per cent. showed albumin some time during the course of the disease. Of 28 cases of varioloid, 60 per cent. showed albumin during the course of the disease.

That the presence of albumin did not indicate merely a febrile albuminuria is evidenced by the fact that casts were found in a considerable proportion of cases. Surprising to relate, the percentage of cases of varioloid in which casts were found is somewhat greater than of variola; 43 per cent. of the 83 cases of variola showed casts in the urine, while of the 28 cases of varioloid 50 per cent. showed casts. The comparative frequency of albumin and casts in fatal cases as contrasted with those that recovered may be seen from the following figures. Of 38 cases of fatal smallpox, 30, or 84.47 per cent., showed albuminuria, and 19, or 50 per cent., showed casts. Of 90 cases that recovered, 45, or 50 per cent., had albumin in the urine, and 41, or 45.55 per cent., showed casts.

It is of interest to note the period at which albumin and casts first appeared in the urine in these cases:

ALBUMIN IN FATAL CASES.

	Cases.
5th day or before . . .	16 or 52 per cent.
6th to 10th day . . .	9 " 29 "
11th to 15th day . . .	3 " 9.7 "
16th to 20th day . . .	0 " 0 "
After 20th day . . .	3 " 9.7 "

CASTS IN FATAL CASES.

	Cases.
5th day or before . . .	9 or 47 per cent.
6th to 10th day . . .	7 " 27 "
11th to 15th day . . .	1 " 5.5 "
16th to 20th day . . .	1 " 5.5 "
After 20th day . . .	1 " 5.5 "

ALBUMIN IN CASES THAT RECOVERED.

	Cases.
5th day or before . . .	24 or 53.5 per ct.
6th to 10th day . . .	12 " 26.6 "
11th to 15th day . . .	4 " 8.6 "
16th to 20th day . . .	4 " 8.6 "
After 20th day . . .	1 " 2.2 "

CASTS IN CASES THAT RECOVERED.

	Cases.
5th day or before . . .	11 or 26.8 per ct.
6th to 10th day . . .	16 " 39 "
11th to 15th day . . .	7 " 17.1 "
16th to 20th day . . .	5 " 12.2 "
After 20th day . . .	2 " 4.8 "

It will be seen from the above tables that when albumin is found in the urine it usually appears early. In over half of the cases in which it was present, it was first discovered on or before the fifth day of the eruption. The onset of albuminuria seemed to be about the same in fatal cases as in cases ending in recovery. Tube casts when present were also found comparatively early. The tables would indicate that in fatal cases they were present at an early period in a larger percentage of cases than in favorable cases. We desire to point out the fact that albumin and casts, singly and together, may first appear in the urine late in the course of the disease, even when convalescence is established.

Another observation of interest is that the urine from day to day will exhibit striking differences. It will be seen from the appended report of cases that albumin and casts were not present daily from the time of first appearance, but at irregular periods. For instance, in some cases the urine would contain albumin and casts for several consecutive days, then perhaps on alternate days, and then the urine might be free of these for a week or thereabouts, suffering a return a few days later. It is evident that a single examination of the urine under such conditions might readily fail to detect the presence of the abnormal urinary constituents. The persistence of albumin and casts in the urine was also most variable. In some cases they would be present only for a few days and would then permanently disappear. In other cases they would persist for two or three weeks or even longer. In at least two cases, both suffering from smallpox with discrete eruptions, tube casts were present in the urine when the patients were discharged from the hospital. Both of these patients were young men and had not had, to their knowledge, any antecedent kidney disease.

It was not uncommon for tube casts to precede the presence of albumin in the urine and to persist after its disappearance. Indeed, in seven cases casts were found in the urine when albumin was absent. This observation demonstrates the inadequacy of the albumin test in determining the presence of disease of the kidneys, and emphasizes the importance of examining the urinary sediment under the microscope.

The occurrence of uræmic seizures in smallpox is extremely uncommon. Convulsions, except during the initial stage, are rarely met with.

To what extent the condition of the kidneys may contribute to the coma that is not infrequently observed in bad cases of confluent smallpox is a question difficult of solution. Edema of the lower extremities is frequently seen during convalescence, but this may be, in at least some measure, attributed to other causes. It may in general be stated that the clinical manifestations of variolous nephritis are much less conspicuous than those characterizing this complication in scarlet fever.

Arnaud¹ made 1248 urinary examinations in 400 cases of smallpox. He states that 95.3 per cent. of these patients had albuminuria. The cases were classified, according to the amount of albumin present, into abundant, moderate, slight, and minimal albuminuria:

a. Abundant albuminuria (above 50 grm. to the litre)	35 cases or 8 per ct.
b. Moderate " (20 to 50 grm. to the litre)	21 " 5.25 "
c. Slight " (0.05 to 20 grm. to the litre)	146 " 36.50 "
d. Minimal " (0.005 to 0.05 grm. to the litre)	100 " 25.00 "
e. Absent	10 " 2.5 "
	400

Arnaud employed delicate reagents² to determine the presence of the minutest quantities of albumin. Other investigators have obtained results which vary greatly. It is evident that the figures would be markedly influenced by the number of examinations made and the delicacy of the tests.

Lyon	found albumin	1 in	50 cases or 2 per ct.
Bourru (Thèse de Paris, 1874)	"	15 "	70 " 22.5 "
Couffiant (Ibid., 1881-82)	"	42 "	114 " 27.2 "
Bourgin (Thèse de Lyon, 1885)	"	77 "	214 " 26 "
Robin (Bull. de l'Acad. de méd., 1898, xx.)	"		30 "
Roger (Maladies infectieuses, Paris, 1902)	"	11 "	35 " 22.5 "

Arnaud remarks upon the daily variations in the amount and in the presence of albumin, and counsels repeated examinations. He furthermore states that albuminuria persisted after convalescence in 75 per cent. of his cases. In other words, three-quarters of the patients when convalescent still had albumin in the urine—to be sure, in minimal quantities in most cases. He contends that variolous albuminuria, like most albuminurias accompanying infectious diseases, is not simply functional, but is related to a structural alteration in the kidneys. In proof of this he cites the results of histological examination of the kidney in 13 cases of smallpox.

He found, even in cases of minimal albuminuria, marked pathological changes in the kidney structure. These organs examined in the acute stages, even in the absence of clinical manifestations of nephritis, presented a constant alteration. The changes were briefly of two types: first, an interstitial cell infiltration, and, second, lesions of the epithelium of the tubules. Albuminuria is slight where the interstitial changes are found, and more abundant where the epithelium is involved. Arnaud believes that in light cases the kidneys may entirely recover, but in most instances a renal defect is left, which, though compatible with a satisfactory physiological state, may under certain conditions be awakened or brought into evidence. Pregnancy, muscular fatigue, alimentation, digestive troubles, etc., may thus excite albuminurias which are often spoken of as physiological, cyclical or intermittent, but which represent in reality a reawakening of a process which had its origin perhaps in some infectious disease.

¹ Revue de médecine, 1898, tome xviii, p. 392.

² Millard's test and the sulphate of soda test.

CHAPTER V.

SMALLPOX (*Continued*).

COMPLICATIONS AND SEQUELÆ OF SMALLPOX.

As would be naturally expected, the skin is most commonly the seat of complications in variola. The secondary pyogenic infection of the skin gives rise, as has already been stated, to *impetigo* lesions. These are so common that they have been described under the head of symptomatology. The postvariolous toxic and septic rashes have also been alluded to under this caption.

Boils constitute the most frequent complicating disorder met with in smallpox. But few patients pass through an attack of variola vera without suffering from numerous furuncles. The subjects of confluent smallpox suffer more severely than those who have a lighter form of the disease. Even patients with varioloid, however, are not always exempted from this troublesome complication. The furuncles develop most commonly after the stage of decrustation, about the twentieth or twenty-fifth day of the disease.

Subcutaneous Abscesses.—Subcutaneous abscesses are commonly associated with the more superficial furuncular inflammations. These may occur upon any part of the body surface, but involve with predilection the scalp, face, arms, and legs. They are often preceded by a cellulitis or a phlegmonous inflammation of the skin and subcutaneous tissues. The patient first experiences soreness and pain in the affected portion of the body. The skin is seen to be swollen, infiltrated, and reddened. In the course of several days, fluctuation may be detected, and on incision large quantities of pus, even as much as a pint, may be evacuated. The entire skin of the leg, arm, or scalp may be extensively undermined by these accumulations. Besides being very painful these purulent collections are accompanied by high fever of a septic type. We have known such a fever to continue as long as one hundred and twenty-six days, the patient ultimately recovering. Sometimes an insignificant and, at times, undiscoverable purulent focus will send the temperature up four or five degrees, whereas in other patients a large abscess may be present without much febrile disturbance.

In confluent smallpox subcutaneous abscesses may destroy life through the production of an intense septicæmia. It is surprising, however, how patients, worn down by a severe and exhausting disease, are frequently able to successfully combat the pus absorption until convalescence is fully established. We recall a young man, who, after a severe attack of smallpox, became the subject of a most protracted series of abscesses.

For six or eight weeks purulent collections, varying in size from a hickory nut to an egg, were almost daily evacuated. The scalp and integument of the face were undermined, the pus communicating with the surface through numerous fistulous openings. No part of the cutaneous surface remained free; in all, this patient suffered from no less than two hundred abscesses. Although greatly emaciated he was subsequently restored to health. Fig. 45 shows the *pseudokeloidal elevations*, made up of hypertrophic granulation tissue, which were left after the healing of the abscesses on the face.

FIG. 45



Pseudokeloidal elevations following abscesses upon the face.

Carbuncles.—Carbuncles may develop during convalescence from smallpox, but in our experience they occur with great rarity. We recall a carbuncle which began upon the back of the neck, about the end of the third week, in a patient who suffered from a well-pronounced attack of discrete variola.

Erysipelas.—This complication, when it develops, usually appears at the end of the second or third week of the disease. The face is the region most often affected, although the process may attack the extremities or trunk. At times a diffuse *erysipelatoïd inflammation* of the skin occurs without the actual development of a true erysipelas. Both of these conditions are attended with high fever which rises in the evening and remits in the morning. During the epidemic of 1901-02, among approximately two thousand cases of smallpox, we encountered about ten instances of erysipelas. Considering the multiple abrasions of the

skin, the lowered condition of the patient's vitality, and the almost constant presence of streptococci on the cutaneous surface, it is surprising that erysipelas does not more often attack the smallpox sufferer. Almost all of our patients who contracted erysipelas recovered; some, however, unable in their exhausted condition to withstand the superadded infection, succumbed to the disease.

Bed-sores.—Bed-sores occasionally occur in the course of smallpox, as they do in other protracted diseases. They are far less frequent at the present time than in earlier days. They result from pressure, malnutrition, and uncleanness, and may usually be avoided by careful nursing.

Gangrene.—At times, during the pustular stage of smallpox, the swelling and inflammation of the skin may be so great as to produce multiple areas of necrosis. Sloughing of the skin may also result from undermining of the integument by subcutaneous abscesses.

Apart from these losses of cutaneous tissue, spontaneous gangrene of the skin occasionally occurs during the course of variola. The genitalia are the parts most commonly involved. *Gangrene of the scrotum* is a complication of great gravity, for most patients thus attacked succumb to the disease. It usually manifests itself first as an œdematous swelling of the scrotum, which is rapidly followed by gangrene. In extensive cases a considerable part of the integument is lost, exposing to view the testicles, which remain unaffected. When this unfortunate accident develops, it begins about the end of the second week of the eruption; it is most likely to develop in bad confluent cases.

Gangrene of the skin is not limited to the regions above mentioned. It may attack almost any portion of the cutaneous surface. During the years 1901 and 1902 we observed three cases of gangrene of the scrotum and five cases in which gangrene occurred upon various portions of the thigh. In some of the latter cases extensive destruction of the cutaneous, subcutaneous, and muscular tissues occurred, the sphacelated areas attaining at times the size of the palm of the hand. In four of the five cases recovery took place after a tedious convalescence. It may be of interest to note that most, if not all, of these patients suffered from a more or less extensive impetigo variolosa. In the malignant epidemic of smallpox in 1871–72 neither impetigo, gangrene, nor the septic rashes were encountered as frequently as during the last epidemic (1901–04). This leads us to emphasize the statement that the character of the disease and the nature and frequency of the associated complications appear to vary greatly in different epidemics.

The Ocular Complications of Variola.¹—Since Jenner's discovery the destructive effects of smallpox on the ocular tissues have been greatly lessened.

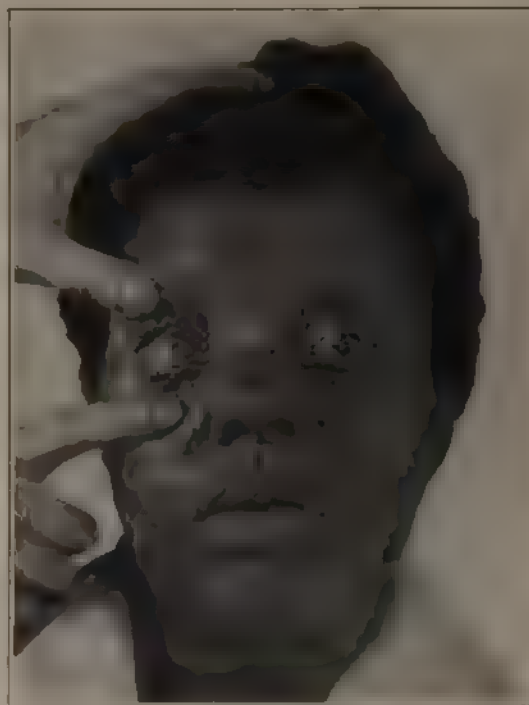
In the analysis of over 2000 cases of smallpox at the Municipal Hospital, in 1901–02, pustulation of the lid borders was a common affection;

¹ The above section on "Ocular Complications of Variola" has been kindly prepared for us by Dr. Burton K. Chance, Assistant Surgeon to Wills Eye Hospital, Philadelphia, and Ophthalmic Surgeon to the Germantown Hospital.

conjunctivitis was frequently found with it and was also found independently. There were 36 instances of corneal ulcer, 17 of which were followed by perforation with destruction of one eyeball, and 15 cases were cured without perforation. Of these cases, 15 were in unvaccinated individuals; in 6 others, vaccinated at periods more or less remote, the lesions were less severe; 10 cases of iritis were especially noted.

In taking up the systematic consideration of the action of variola on the various parts of the eye, we find that the skin of the lids is commonly a site of the pustular eruption. So much swelling of the tissue may

FIG. 46



Destructive corneal ulcer with panophthalmitis occurring in the latter stage of severe smallpox

accompany the eruption that the eyes cannot be opened for several days. In such cases severe *conjunctivitis* is usual and often leads to corneal ulceration. The edges of the lids are liable to ulceration and the subsequent cicatrization distorts them, so that styes, misplaced cilia, eversion of the lids, or occlusion of the Meibomian ducts, etc., may result. The lids, like other portions of the skin, after the subsidence of the eruption, may be the seat of abscesses which produce various deformities requiring operation later. As to the mucous membrane of the lacrymal passages, pustules may also form there and give rise to acute and, later, chronic inflammation of the canal and duct. On the orbital borders periostitis with caries occurs but rarely.

Passing on to the conjunctiva, we find that, as in other febrile diseases, it is commonly affected. Inflammation develops about the fifth day of the eruption; the conjunctiva appears congested and occasionally presents a catarrhal inflammation which is usually of moderate severity and of brief duration, yielding in a few days to treatment. An exception to this appeared in a young man under our care, in whom severe conjunctivitis began on the seventh day, and, in spite of careful treatment, persisted over a month.

The intensity of the ophthalmia is related directly to that of the pustular eruption in general, and more particularly to that of the eruption on the face and eyelids. On the conjunctiva pustules form but rarely; among the 2000 patients with variola, examined by us in 1901 and 1902, they were noticed in only two or three instances. When they do occur, these pustules much resemble in appearance and course the phlyctenular eruption observed in strumous children. They are the size of small lentils, elevated but slightly, and usually situated midway between the corneal margin and the inner and outer canthus. They appear sometimes at the limbus, and when there frequently cause ulceration of the cornea. On the tarsal conjunctiva pustules may be found at the inner fold and on the caruncle, but never at the fornix. In these cases the conjunctival inflammation markedly resembles that of gonorrhœal infection; the inflammation is always severe and is accompanied by profuse secretion and chemosis.

Subconjunctival ecchymosis may occur and may produce intense chemosis in hemorrhagic variola. The bacteriological examination of the conjunctival secretions showed the presence of no specific or hitherto undescribed organisms, but there were present in abundance staphylococci, streptococci, and pneumococci.

The cornea, according to other observers, is not subject to the specific lesions of variola, and our experience would lead us to accept this conclusion. Among over 9000 cases of smallpox we have never seen a variolous vesicle or pustule on the cornea. *Ulceration of the cornea* does occur, but it is usually independent of the general process, being rather a consequence of the conjunctival affection. And now, just as in past times, it is the most fruitful cause of blindness as a sequel of variola.

During a period of over thirty-five years but two persons suffering from smallpox have left the Municipal Hospital totally blind. Quite a number would, however, have been sightless had recovery taken place.

The corneal complications may arise in two ways: first, either without pustules on the conjunctiva or by pustulation, especially when this is at the limbus; second, at about the fourteenth or fifteenth day of the eruption, during the stage of desiccation, when the infection is transmitted from some broken-down pustules, as, for instance, those of the skin of the eyelids.

The corneal inflammation may be only a slight superficial haze confined to the corneal conjunctiva or Bowman's membrane, or it

may extend rapidly and involve the entire membrane. Commonly near the margin of the cornea is seen a small, phlyctenular bleb, filled with clear fluid, the thin and delicate covering of which is soon macerated by the increased conjunctival discharge, and the vesicle is ruptured, exposing an area of necrotic tissue of grayish color. The symptoms of pain and redness, although usually marked, vary in intensity and duration. As the ulcerated surface spreads the several layers of the cornea are involved until the membrane is perforated, and the aqueous humor escapes and prolapse of the iris follows. At this time the painful symptoms abate. In bad cases pus forms in the anterior chamber or the crystalline lens, and the vitreous humor may be extruded, panophthalmitis developing from a general suppuration of the eyeball, accompanied by great pain, with marked bulging of the lids. Fortunately, the majority of cases present a milder form of keratitis. In this there is only a circumscribed superficial inflammation, which heals promptly and leaves the eye damaged only by the formation of an opacity as the result of the cicatrization of the necrosed area. These scars cause marked irregular astigmatism, which greatly interferes with the acuteness of sight.

In severe cases of confluent variola rapid destruction of the cornea may take place as early as the eighth day. It is usually a forerunner of fatal collapse. In some instances both eyes are affected. As an example of this, four patients in our own wards sank rapidly after the destruction of both eyes, at an early stage of the general disease. In these cases it was noted that the ulceration was preceded by a grayish infiltration of the bulbar subconjunctival tissues; this chemosis rapidly increased, rising above the cornea and surrounding it, choking off its circulation. Immediate destruction of the cornea followed—a true keratomalacia. In certain instances the chemosis is so great as to produce an edema of the subconjunctival and subcutaneous tissues, even to such an extent as to make it almost impossible for the lids to be opened.

It has been our experience to find the ulceration of the cornea less extensive in size and degree in patients who have once been vaccinated; consequently, in such persons, the healing is more prompt and the sequelæ are less damaging to the integrity of the eyeball.

Parenchymatous keratitis after variola has been reported by but few observers. We observed two cases. The first was in a young man with confluent variola, who developed about the seventeenth day a general haziness of the left cornea. This gradually improved, leaving a slight opacity behind it. About two weeks later an ulcer developed upon this site, without, however, producing serious complications. The second was in a young woman, aged nineteen years, previously of apparent robust health. With her, marked corneal haze was noticed in the third week of the general disease. Her convalescence was prompt, yet on discharge from the hospital there was noticed well-defined interstitial infiltration and iridocyclitis associated with it. For two months she was under treatment and her progress toward recovery was rapid.

The uveal tract is not so frequently affected as the cornea. In our examinations we noted ten cases of *iritis*, not plastic in form, but of the serous type; it usually manifested itself from about the ninth to the nineteenth day of the eruption. Other observers have noted *iritis* developing after the subsidence of the general symptoms. Slight pericorneal injection was noticed sometimes in the first week, accompanied by lacrymation, photophobia, tenderness, and a small immobile pupil. Although this ciliary irritation may be an independent affection, it is usually a symptom of corneal or iritic disease. It appears to be more frequent in the milder cases, and may persist for a considerable time after the termination of the attack of variola.

Choroiditis was revealed only by the presence of opacities in the anterior or posterior part of the vitreous. We had the opportunity of studying the ocular conditions of a vigorous young man for several weeks after his discharge from the hospital; in each eye were numerous floating vitreous opacities, which rapidly lessened as he regained strength. In none of the cases examined did we find circumscribed choroidal inflammation, nor did we see posterior polar cataract. We can report no cases of glaucoma due to variola, nor any cases of retinitis or neuroretinitis. But all these have been reported in the literature of variola by other observers.

In hemorrhagic variola there is no reason to doubt the occurrence of hemorrhages into the retinal sheet, and very probably hemorrhages into the optic nerve may occur. We have not been able to find any such cases reported as actually observed, but Knies is of the opinion that such hemorrhages must have been the cause of some of the affections described as neuritis with and without stasis (choked disk), and with and without termination in atrophy of the optic nerve.

Meningitis as an undoubted sequel is rarely found, but we have come in contact with cases of meningitis for which no logical cause could be found except a remote attack of variola.

Ear Complications.—The pinna of the ear and the external auditory canal frequently exhibit numerous lesions of smallpox. During the stage of pustulation hearing may be impaired through obstruction of the canal by swelling caused by the presence of the eruption.

Otitis media is occasionally produced by extension of inflammation from the throat along the Eustachian tube. Upon rupture of the tympanic membrane a foul-smelling pus is copiously discharged. One or both ears may be involved. While this complication is rather unusual in adults, it is commonly seen in children. A young boy under our care, suffering from a severe purulent inflammation of the middle ear, developed a *paralysis of the facial nerve* on the same side. This was doubtless due to extension of inflammation to the nerve as it traverses the bony roof of the middle ear.

When *otitis media* develops it usually manifests itself during the suppurative or desiccative stage. Often before attention is directed to the ear, a sharp rise of temperature occurs. More or less permanent impairment of hearing may result from this suppurative inflammation.

Writers have recorded instances in which extension of the inflammation has led to caries of the petrous portion of the temporal bone, and in other cases to thrombosis of the sinuses of the brain.

Respiratory Organs.—Reference has already been made to the symptoms produced by the presence of the eruption in the larynx. When the lesions in the neighborhood of the vocal cords are numerous, *œdema of the glottis* may develop, in which event death almost invariably follows. At a later period of the disease, at times during convalescence, ulceration of the larynx may occur with the production of a *perichondritis laryngæ*. This complication is fortunately of great rarity.

The presence of variolous lesions in the trachea and bronchial tubes leads to the production, respectively, of a *tracheitis* and *bronchitis*, characterized by considerable cough and expectoration of mucopurulent material. These symptoms are present to a moderate extent in most well-pronounced cases of smallpox.

Lobar Pneumonia.—We have found *lobar pneumonia* to be a rather rare complication of smallpox. During the years 1901-02 we observed but one frank case among two thousand patients. *Catarrhal pneumonia* has likewise been infrequent in our experience. A patient who presented for some days a patch of dulness over the base of one lung was, at a late stage of the variolous disease, suddenly seized with severe pain in the chest and great dyspnoea; he rapidly sank, and died on the following day. Autopsy disclosed the presence in the lung of a large, egg-sized cavity with a softened and ruptured wall. This probably resulted from the breaking down of a *pulmonary infarct*. The pleural sac contained a considerable quantity of bloody fluid.

Pleurisy.—Of the internal structures, the pleura, perhaps, is most disposed to take on inflammatory action. When pleurisy occurs, we usually have the symptoms well marked; yet at times a latent form of the disease may exist, of which the patient makes no complaint, and which may be wholly overlooked until death, when a post-mortem examination will reveal a pleural cavity filled with a seropurulent material. Acute pleurisy occurring during the decline of the eruption sometimes proceeds rapidly to *empyema*. We recall a patient from whom nine pints of pus were removed by aspiration, but who later succumbed to this complication.

Myocarditis.—It is but natural in a disease of the nature of smallpox that inflammatory and degenerative changes should take place in the heart muscle. The myocardial disease may result from the pyrexia, the variolous poison, or the associated infections, or from a combination of these. *Pericarditis* and *endocarditis* are encountered with great rarity.

Curschmann remarks having seen an ulcerative endocarditis in a case of confluent smallpox. We observed an ulcerative endocarditis on autopsy in a woman who was sent into the hospital with a poorly developed varioloid, and who died a few days after admission. It was evident that the endocardial disease had antedated the smallpox.

Phlebitis.—Phlebitis and venous thrombosis may be met with as a sequel of variola, especially in the lower extremities, giving rise to phlegmasia alba dolens.

Joint Disease.—Joint disease occasionally occurs as a complication or sequel of smallpox, particularly in children. One or more of the joints may become swollen and painful. The elbows appear most likely to suffer. Chondritis and osteitis may occur, followed by suppuration and destruction of the joint and frequently by death. Neve has reported a number of cases of joint and bone disease following smallpox in children, and we have likewise met with a few such cases.

Abdominal Complications.—Smallpox is singularly exempt from abdominal complications. *Diarrhæa* not infrequently occurs as the result of some derangement of the digestive function. While this symptom is usually controllable, it may occasionally be so severe as to precipitate a fatal issue in those greatly weakened.

Peritonitis is a rare complication, and when it occurs may be attributed to some local cause.

Orchitis.—We encountered this complication in perhaps six or eight patients during the first two years of the epidemic of 1901–04. The swelling may involve the entire scrotum or may be limited to the testicle and epididymis. One or both organs may be affected. The parts often become extremely firm to the touch. The enlargement commonly persists for a few weeks and then gradually subsides, although a variable amount of infiltration may continue for a much longer time. A young man recently under our care had a severe confluent smallpox, complicated by gangrenous inflammation of the arm, iritis, and orchitis. The right testicle was swollen to three times the size of the left. The swelling was firm and not very painful. The infiltration, which extended along the spermatic cord to the external abdominal ring, reached the diameter of an adult thumb. It is said that the analogue of this condition, *ovaritis*, may develop in the female. We have never observed any symptoms during an attack of smallpox pointing to acute disease of the ovaries.

Phimosis.—Phimosis not infrequently occurs in the pustular stage of smallpox as a result of the swelling of the areolar tissue of the prepuce occasioned by the presence of the eruption. This is seen most commonly in young children.

Nervous System.—Psychic disturbance in the form of *delirium* is not uncommon in the early eruptive period of smallpox. It may in some cases supervene at a later period of the variolous process. The delirium may persist for some days and then disappear, or in rare cases it may develop into a *confusional insanity*. The following cases of insanity after smallpox have come under our observation:

E. M., aged twenty-eight years, was admitted to the Municipal Hospital on November 29, 1903, with smallpox. She bore one good scar from a vaccination in infancy and had a well-marked, discrete variola. On December 6th she was observed to be delirious at times. The mental excitement increased and the patient became maniacal

and had to be strapped in bed. From this time on there were occasional lucid moments, but for the most part the patient was delirious. She would sing and cry and appeared to be completely demented. Despite the fact that the variolous symptoms had quite subsided, the patient continued to lose weight and strength and died in an insane condition, apparently from exhaustion, on January 24, 1904, two months after the onset of the attack of smallpox.

Mrs. A. C. was admitted to the Municipal Hospital on March 10, 1904, with a modified attack of smallpox. She bore two good vaccination scars from infancy. The patient had never exhibited any mental disturbance before the attack of smallpox. Family history negative. On admission the patient exhibited evidences of mental disturbance. She spoke at times rationally, but for the greater part talked incoherently and almost exclusively upon religious topics. Later she became maniacal, jumped from the bed and through an open window; she had to be strapped to her bed to prevent violence. At times refused to eat or drink. She later, when released from her bandages, made several more attempts to jump through the window. She was removed to her home on April 9th, her mental condition having remained unchanged.

Another patient, L. E., aged thirty-seven years, who had recovered from a mild attack of smallpox, developed religious mania after convalescence. He was transferred to a hospital for the insane. It was subsequently ascertained that he had, before his attack of smallpox, suffered from a similar mental disturbance.

Several cases of insanity after smallpox are reported by Seppilli and Maragliano. Of three instances referred to, one remained permanently insane, the others recovering after appropriate treatment. The authors also record the remarkable case of a violent maniac, who had been confined for about six weeks in an asylum, who during an attack of confluent smallpox was restored to his senses and after convalescence from variola was discharged from the asylum as a sane man.

Brain symptoms sometimes appear during the stage of decline. We cannot recall a single instance where we have observed clear and indubitable evidence of acute inflammation of this organ, yet we have seen a few cases—perhaps not more than three—lapse into a state of lethargy or coma, when desquamation had almost completed, without evincing any preceding symptoms of inflammatory action. We have met with a few cases in which there were peculiar psychic changes, followed by *aphasia*. This condition we attributed to the presence of a circumscribed encephalitis. Westphal has called attention to cases of similar nature. In 1872 he presented before the Berlin Medical Society a patient, who during smallpox had had attacks of delirium or coma, followed by a curious disturbance, characterized by slow, measured, scanning speech, and ataxia of the upper and lower extremities, similar to that seen in *tabes*.

Paralysis.—Various paralyses may develop during the course of variola. During the past few years we have observed eight instances

of paralysis among about 3000 cases of smallpox. Of this number five died and three recovered.

In an infant, one year and four months of age, we observed a *hemiplegia* occur upon the first day of the eruption. This succeeded repeated convulsions which took place immediately before and after the appearance of the exanthem. It is probable that this condition was not intimately connected with the variolous process, but resulted from a brain hemorrhage excited by the convulsive paroxysms.

In another patient, a woman, paralytic symptoms appeared during the initial stage of the disease. She was brought into the hospital in a stuporous state, barely able to articulate. There was great difficulty in swallowing and impaired power in the arms and legs; the loss of power in these members subsequently became almost complete, but later a gradual restoration of function occurred. The patient had a most pronounced scanning speech, which was still present when she was discharged from the hospital. The reflexes were markedly exaggerated.

The third patient, a young colored man, had a severe attack of smallpox, complicated by extensive gangrene of the scrotum and penis. At the end of about ten weeks from the onset of the disease he developed partial loss of power in the legs and arms. He could walk with great difficulty with a cane. This condition persisted to the day of his departure from the hospital.

Sometimes the spinal cord is preponderantly or exclusively affected, the symptoms being those of a *paraplegia*. We have observed a half-dozen or more instances of this serious complication, of which the following are of especial interest:

CASE I.—C. M., aged thirty years; unvaccinated; was seen in consultation on April 22, 1902, on the first day of the smallpox exanthem. The eruption was confluent on the face and hands, and covered thickly all parts of the body.

The pustules began to shrink on the eleventh day; the secondary fever was not high, and there was no delirium. The patient was progressing favorably until May 4th, when it was found that he was unable to void his urine, necessitating catheterization. On the following day paralysis of the lower extremities was noted, sensation being, however, preserved. There was also complete loss of power over the bowels and bladder. Immediately preceding the paralysis, there were hebetude and drowsiness, which persisted for several days. A week later, on May 12th, slight motion returned in the legs. A gradual improvement in all of the symptoms then set in. By June 23d the patient was able to walk a few blocks without difficulty, although control over the bladder and rectum was not quite perfect. Complete recovery ultimately resulted.

CASE II.—Mrs. N., married, aged nineteen years, was admitted to the hospital with a smallpox of considerable severity. She was progressing well when during the third week of the disease she became unable to move her legs. Sensation was impaired, but not entirely lost. She had loss of control of the bladder and rectum. Within a few days

al motion was restored in the lower limbs. Later diarrhoea set in the patient died.

CASE III.—J. W., a man aged thirty-eight years, was admitted to hospital on January 13, 1903. He had a scant, modified eruption, been vaccinated in infancy. About a dozen lesions were present on the anterior surface of the body, a few were scattered sparsely on the extremities, and on the face there were about fifty lesions.

On the eighth day of the eruption the patient developed loss of power in his legs so that he was unable to raise them from the bed. Sensation was impaired, but not lost. There was no pain. The mental condition was good. Later, retention of urine developed, followed after some days by incontinence of urine and feces. The patient died on the thirty-sixth day of the disease, after ten days of high and irregular fever.

Autopsy disclosed the existence of a number of abscesses in the kidneys. A culture from the intradural fluid in the spinal region revealed the presence of staphylococci.

The cord from this patient and from Case II. were sent for study to Prof. W. G. Spiller,¹ of the University of Pennsylvania. The spinal cord from Case II. had been hardened in alcohol and the microscopic study was, therefore, unsatisfactory, although nothing distinctly abnormal could be detected in the cord.²

In regard to Case III., Prof. Spiller states: "Strictly speaking, the case was one of diffuse myelitis, but with the exception of a part of the thoracic cord the myelitis was almost confined to the anterior horns and was an anterior polyomyelitis, and probably of vascular origin."

Grave Lesions of the Nervous System Complicating Smallpox with but Scant Eruption.—It would appear that in rare cases the poison of smallpox is largely expended upon the nervous system, the skin escaping with very few lesions. These cases are an exception to the general statement that the gravity of smallpox is proportionate to the extent of the eruption. A remarkable case of this character came under our own observation during the year 1902.

E. M., a burly negro, aged twenty-seven years, was admitted to the hospital on April 7, 1902. The patient had never been vaccinated. According to the history, the initial symptoms had been well marked—headache, vomiting, fever, and backache having been present. The entire eruption consisted of about a dozen small papules, scattered over the face, forearms, hands, and trunk. These were arrested in their development and dried up in a few days, as occurs commonly in cases of varioloid. The patient fell into a state of hebetude after admission, although he had walked to the ambulance. He became progres-

¹ Prof. Spiller reported the full findings in these cases in a paper entitled "A Report of Two Cases of Paraplegia Occurring in Variola, One being a Case of Anterior Poliomyelitis in an Adult." Other cases in the literature of the subject are referred to. Brain, Autumn, 1903, London.

² Since the above chapter was written an article on "Nervous Complications and Sequelae of Smallpox," by Dr. Charles J. Aldrich, has appeared in The American Journal of the Medical Sciences, February, 1904. The author reports three interesting cases of aphasia after smallpox, and carefully reviews the entire subject, giving a full and extensive bibliography.

sively more stuporous, had difficulty in swallowing, and partial anæsthesia and loss of power in the legs. Later, complete paraplegia with incontinence of urine and feces developed. He died on the fourteenth day of the eruption. The temperature on admission (third day of eruption) was 99.2° F.; it later fluctuated for nine days between this point and 101° F., rising to 104° F. just before death.

The diagnosis of smallpox, owing to the poorly developed lesions, was not entirely certain until about ten days later, when the wife and child of the patient were brought into the hospital with variola. Autopsy showed great softening of the spinal cord in the region of the lower dorsal and upper lumbar vertebræ. When the dura over this area was punctured the softened cord ran out like pus. From this portion of the cord a micrococcus was grown on culture. The brain showed no gross changes save an intense congestion of the pia mater.

It is interesting to note that in one of the cases of paraplegia reported by Westphal the patient had an extremely scant eruption and the "disease was so mild that the patient did not go to bed." MacCombie has also called attention to serious disease of the nervous system developing in the course of mild cases of smallpox.

Peripheral Neuritis.—Peripheral neuritis is encountered as a complication or sequel of smallpox with great rarity. In the case of paraplegia, to which we have already referred, in which no microscopic changes were found in the cord, the lesion may have been a peripheral neuritis. Combenale believes the disorders of speech occasionally complicating smallpox to be due to paralysis resulting from the action of toxins upon the peripheral nerves.

Disseminated Spinal Sclerosis.—An interesting case of typical infectious disseminated sclerosis is reported by Sottas. A young man, aged eighteen years, with a discrete smallpox eruption, presented during his illness most severe nervous symptoms. The patient was semicomatose, had a slow dragging speech, nystagmus, general paralysis, atrophy of the muscles of the trunk and limbs, and later contractures. At a subsequent date there were characteristic tremors, exaggerated reflexes, incoordination of voluntary movements, and great mental excitability.

Septicæmia and Pyæmia.—Septicæmia is commonly observed in the stage of decrustation in confluent smallpox. In severe cases there may occasionally be seen during the third week a high and irregular fever, rapid pulse, low delirium, and great prostration, without there being discoverable any pus collection to account for these symptoms. Pyæmia is more rare than would be supposed from the writings of the older physicians. Abscesses in the liver, kidney, and lungs have been revealed by autopsies, but with great infrequency.

THE PATHOLOGY OF SMALLPOX.

The Histopathology of the Pock.—The microscopic structure of variolous lesions has been studied by Bärensprung,¹ Auspitz and Basch,² Ebstein,³ Rindfleisch,⁴ Unna,⁵ Weigert,⁶ Touton,⁷ Renaut,⁸ Leloir,⁹ Buri,¹⁰ and others.

Weigert regarded the primary changes in the epidermis as necrobiotic and diphtheroid, due to the local effect of the smallpox poison. He claims to have found analogous alterations in the liver, spleen, kidneys, and lymph glands, which he believes to be specifically variolous.

Nearly all of the other writers mentioned describe the early changes in the skin as *inflammatory* in character.

According to Bärensprung, cited by Curschmann, the red spot, which represents the first clinical evidence of the pock, is produced by a circumscribed hyperæmia of the papillary and deeper bloodvessels. The papule is formed by peculiar changes in the cells of the mucous layer or the rete Malpighii, which become œdematous, enlarged, and granular. The vesicle is explained by an exudation of clear fluid from the papillary bloodvessels, separating the cells above referred to. It is evident from later studies that other important processes (subsequently to be described) enter into the formation of the vesicle.

The older writers believed the umbilication to be due to a hair follicle, sweat duct, or epithelial strand holding down the centre of the roof of the pock. Auspitz and Basch first pointed out that it was in reality due to the periphery of the pock swelling more rapidly than the centre. This view is corroborated by Unna, of Hamburg.

Unna has carefully studied the structural changes in the skin, employing the most modern histological technique.¹¹ The following description is condensed from Unna's detailed account:

The development of the variolous vesicle is the result of certain peculiar degenerations of the protoplasm of the epithelial cells. The main features which differentiate the vesicle formation in smallpox from that in chickenpox are the slowness of growth and the prompt addition of suppuration to the epithelial degeneration.

The changes in the protoplasm of the cells of the mucous layers of the epidermis are of two chief varieties. These have been designated, by Unna, *reticulating* and *ballooning* colliquation (softening). Both are special forms of *fibrinoid degeneration*.

Reticulating colliquation occurs as follows: As a result of the poison of the disease the protoplasm of the cells becomes œdematous and

¹ Die Haut-Krankheiten, 1854.

² Ibid., Bd. xxxiv., S. 598.

³ Virchow's Archiv, Bd. lxi., S. 409.

⁴ Anat. Beiträge zur Lehre von den Pocken, Breslau, 1874, Heft 1.

⁵ Vergleichende Untersuch. über die Entwick. von Blasen in der Epidermis, 1892.

⁶ Archives de la dermat. et de syph., 1881.

⁷ Archives de la physiol. norm. et pathol., 1880, p. 307.

⁸ Monatshfte f. prakt. Dermat., 1892, Bd. xiv., 1892.

⁹ Histopathology of Diseases of the Skin. Translated from the German by Dr. Norman Walker, 1896.

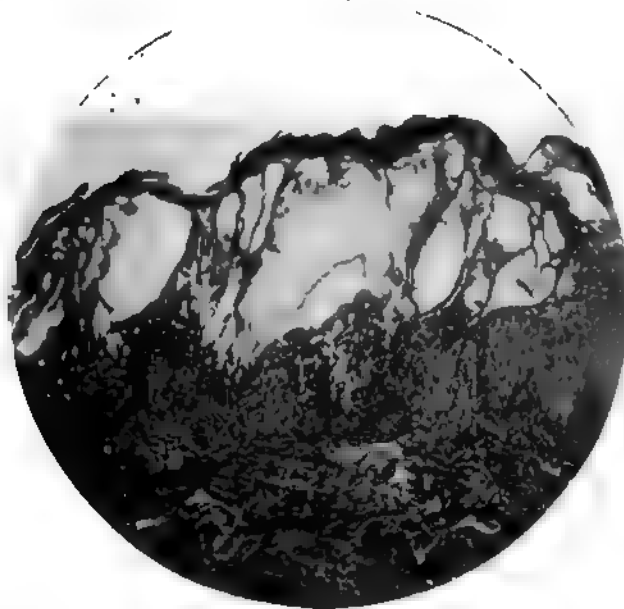
¹⁰ Virchow's Archiv, Bd. xxviii., S. 387.

¹¹ Handbuch der pathol. Gewebelehre, 1871.

undergoes partial or complete liquefaction, thus converting the cell body into a large cavity. Coagulation of the albuminoid bodies set free from the protoplasm now takes place, leading to the formation of a fine granular precipitate which lies on the well-preserved nucleus or the thin, distended cell wall. The nucleus at first remains healthy, but later shows fibrinoid degeneration. When the liquefaction of the cells is partial, protoplasmic trabeculae form which coagulate into a network, often radially arranged, and hold the nucleus and cell mantle together.

The name "reticulating" colliquation is given to this degeneration because of the net-like character of the structure.

FIG. 47



Microphotograph of smallpox pustule showing reticulating epithelial bands. Magnified 80 diameters.

This form of degeneration corresponds with the "alteration cavitaire" described by Leloir and Renault. Leloir maintained that the cavity formation invariably began with a dilatation of the nuclear cavity; in other words, as a result of the liquefaction of the endoplasm.

In the second form of fibrinoid metamorphosis—that designated *ballooning* colliquation—the whole protoplasm of the cell swells up and becomes cloudy and opaque. The prickly projections are withdrawn and the cell becomes rounded. The shape of the cell is largely determined by its position and external pressure, and may be round or flat, biscuit-shaped, pointed, or drawn out into septæ, or bands. Most of the cells, however, have the form of hollow spheres or balloons, the predominance of which gives rise to the name "ballooning colliquation."

The reticulating degeneration mainly attacks the older cells, or those in the upper strata of the Malpighian layer, and the ballooning degeneration the younger cells, or those in the lower strata. This is accounted for by the fact that the younger epithelia contain a homogeneous protoplasm which readily undergoes homogeneous swelling and coagulation, whereas in the older cells a marginal layer separates from the rest of the protoplasm in its preparation for cornification.

Formation of the Smallpox Vesicle.—During the papular stage the cavity formation begins in the upper prickle-cell layer of the epidermis by a reticulating colliquation of the œdematous epithelium. Owing to the slow advance of this process some of the cells are compressed and thus part of the cavity is, from the commencement, divided by septa into a series of segments, the bands running perpendicularly in the centre and being directed outward at the periphery.

At the same time the cells of the lower prickle layer undergo ballooning colliquation. The cells lose their prickles and become detached from one another.

As the pock spreads peripherally the differentiation of the process in the upper and lower strata of the prickle layer becomes more marked. In the upper part the cavity extends laterally, many of the marginal cells liquefying and communicating with the general cavity. In the lower part, on the contrary, ballooning and swelling of the cells develop slowly.

At the height of the development, therefore, the pock has the shape of a mushroom, the main cavity formation taking place in the upper projecting parts, while the under half is sharply constricted.

The cavity is completed by extension of the reticulating degeneration downward, particularly upon the periphery, and by the ballooning and detachment of the deeper cells; the latter subsequently become transformed into the compressed bands which traverse the lower portion of the pock.

Umbilication.—Exceptionally a sort of umbilication may result from the accidental piercing of the centre of the pock by a hair follicle, the cornified neck of which limits the swelling of the prickle cells. The characteristic depression in the centre of the vesicle is due, however, to another cause. It is the result of the reticulating degeneration and œdematous swelling of the cells. These occur chiefly at the periphery, whereas the ballooning degeneration which occurs slowly and gives rise to less swelling takes place in the centre. The umbilication is, therefore, due rather to a *bulging of the periphery of the vesicle* than to a retraction of the centre.

The pressure of the lateral œdematous cells is so great as to lead to obliteration of the underlying papillæ, while in the centre of the pock, before suppuration begins, they not only persist but project into the cavity of the pock.

During the vesicular stage the dilatation of the papillary bloodvessels beneath the pock is slight and the emigration of leukocytes is strikingly small. A dense collection of plasma cells is seen in the sheaths of the

vessels and increases in number as the vesicle matures. This abundance of plasma cells is remarkable, considering the acuteness of the process, and is only found among the pock-like processes in variola itself.

After the fifth day, the bloodvessels, superficial and deep, become distinctly dilated and a stream of leukocytes is poured out, doubtless attracted by the dead germs in the tissues. The margin between the corium and epidermis is so densely packed as to be scarcely recognizable. The cavity of the pock gradually fills up completely with these white blood cells. If the horny roof holds, the mass is converted almost into solid tissue; if it ruptures, there is more or less profuse suppuration, leading to the formation of crusts.

The primary pustulation is due to the variolous poison, but prolonged suppuration must be ascribed to secondary pyogenic infection.

Healing.—Even before the contents of the pustule are completely dry, a thin layer of epithelial cells lying close on the connective tissue extends from all sides under the pustule.

When the scab is thrown off there is displayed a persistent trough-like depression. Where the scab does not to any great extent depress the base of the pock, the papillary layer is not completely flattened out, and the scar is not so deeply excavated.

“The depth of the scar consequently depends on the degree and duration of the flattening of the base of the pock beneath the pustule and the scab, and we see therefore that the rational treatment to avoid scars should be mainly directed to the aborting of the pustular stage and the rapid removal of the scab by profuse epithelial new-growth. . . . Suppuration alone causes no necrosis of the papillary body, but it may, if profuse, lead to a more rapid casting off of the scab, and thus indirectly to the freeing of the base of the pock; the profusely suppurating cases of smallpox are not those which leave the worst scars. No doubt prolonged suppuration, coupled with inappropriate treatment, scratching, etc., may lead in many cases to a purulent sequestration of parts of the cutis and thus to distinct scar formation.”

For a long time the bloodvessels and all the lymph spaces of the cutis are dilated, and wandering cells and pigment are more abundant than normal.

The pocks upon the *palms* of the hands and *soles* of the feet develop in a somewhat different manner from those elsewhere. The reticulating and ballooning degenerations are only imperfectly seen here.

The “pock body” is usually fan-shaped, undergoes a drier degeneration, and has a horny character. It is usually more superficially situated in the epidermis.

Stokes¹ believes that “the primary exudation of plasma cells has not been sufficiently emphasized by Unna. These plasma cells are probably derived in part from proliferation of the endothelial lining of the lymph spaces and bloodvessels. In some sections made from very early cases, the epithelial cells do not show any great injury, but the cutis

¹ The Pathology of Smallpox, Johns Hopkins Bull., No. 149, Aug., 1903.

is swollen and there is increased number of plasma cells in the lymph spaces and around the small bloodvessels. The condition resembles the response to some injury and seems to be the *first change in the skin*, since the various changes in the epithelial cells are not yet present."

In a hemorrhagic case Stokes found the capillaries and lymph spaces greatly distended and numerous hemorrhages present in the connective tissue.

Quite recently careful and extended studies of the pathology and etiology of variola have been carried on by Prof. Councilman,¹ of Harvard College, and a number of his associates.

The anatomy and histology of variolous lesions were investigated by Councilman, Magrath, and Brinckerhoff. Eight sets of complete serial sections were made through typical vesicles and pustules. In the main Unna's findings are confirmed, but some new facts concerning the histology of the pock are presented.

The earliest form of degeneration is said to take place in the nuclei of the cells of the rete mucosum. They become swollen, more vesicular, and exhibit an increased central clumping of the chromatin. In the lesions leading to vesicle formation there is a reticular degeneration of the cytoplasm, with a more advanced degeneration of the nucleus. The nuclei may lose their form and become irregular and shrivelled, assuming peculiar shapes. Advanced forms of cytoplasmic inclusions are common in the nuclear space and in vacuoles in the protoplasm. The protoplasmic processes connecting the cells disappear, but the periphery of the cells remains and undergoes condensation.

It is this degeneration which causes the peculiar reticular appearance of the early vesicle. It is always better seen in the periphery than in the centre of the vesicle. With the increase of the exudate coming from below, the spaces within the cell enlarge, finally rupture, and a network is formed by the coalescence of the cell borders. The typical small vesicle is always fan-shaped, with the handle of the fan seated upon the corium.

A later form of degeneration, the ballooning degeneration of Unna, may best be regarded as a hyaline fibrinoid degeneration. The Malpighian cells become swollen, lose their granular character, become homogeneous and refractile, and stain more intensely with the acid dyes.

The fluid exudate begins early, and in most cases simultaneously with the degeneration. In the smallest visible papule the swelling is due chiefly to the presence of exudate; in no case was degeneration found without evidence of exudation. The early exudate is clear and contains no admixture of cells. Indeed, a conspicuous feature of the smallpox process everywhere is the paucity of cells in the exudate. The cells appear only at a late stage of the process, and are much less than in other degenerations and exudations due to bacterial infection.

¹ Studies on the Pathology and Etiology of Variola and Vaccinia; from the Sear Pathological Laboratory, Harvard Medical School; published in the Journal of Medical Research, February, 1904.

It seems probable that the cells appear when the specific character of the process is passed, they being then attracted to the necrosis. Different varieties of leukocytes are present, but the polynuclear neutrophiles predominate. In the late lesions there are accumulations around the vessels of the varieties of lymphoid cells which are so prominent in lesions in the internal organs, and which Unna has indentified as plasma cells.

During the process of repair the contents of the pustule undergo condensation from the evaporation or absorption of the fluid, becoming finally changed into a solid granular mass in which nothing can be recognized. A complete regeneration without cicatrization is possible when the lesions are not extensive and do not involve the entire epithelium, and also when the entire epithelium is destroyed over a small area only, the papillary bodies remaining intact. When destructive changes in the corium occur, complete regeneration cannot take place. After recovery the papillæ are absent or very imperfectly developed and the connective tissue beneath has the characteristics of cicatricial tissue.

Councilman, Magrath, and Brinckerhoff believe that Weigert's explanation of the cause of the *umbilication* is correct in many instances. Weigert regarded the umbilication to be due to the diphtheroid degeneration of the epithelium of the centre of the vesicle, thus preventing the distention of the centre by the exudate; he believed, however, that the hair follicles and sweat ducts also played a part in its formation. The above-mentioned investigators cannot attribute the umbilication to any single cause. In serial sections the presence of hair and sweat glands at the point of umbilication was rarely missed. The hair follicles play a more important role than the sweat glands. Nevertheless, they are not exclusive agents in the umbilication, for lesions are frequently present upon the glans penis. It is suggested that two factors may combine to favor umbilication: a naturally more resistant centre (doubtless due to the degenerative changes), and in some cases the presence of a hair follicle or duct which further strengthens the centre.

Histology of Purpura Variolosa.—The skin of four cases of purpuric variola was examined by Councilman, Magrath, and Brinckerhoff. Although diffuse hemorrhages were present, the skin almost everywhere showed the early changes characteristic of the variolous process. The general condition was that of swelling and reticular degeneration of all of the lower cells of the epidermis. There were large vacuoles in the cells, but rarely spaces between the cells resulting from their rupture. In the Malpighian layer there was some separation of the cells by the exudate, and in one section the entire epidermis over a small area was separated from the corium. The nuclei were degenerated, shrunken, and lay in large spaces.

The corium showed dilatation of the bloodvessels and hemorrhages, chiefly in the papillary layer. The most striking condition found in the corium was the presence of large numbers of streptococci in the bloodvessels and lymphatics and in the tissues. No polynuclear leukocytes were found in the epidermis, and but few in the corium.

Mucous Membranes.—As has been stated in the chapter on symptomatology, certain of the mucous membranes participate in the variolous process and show the presence of pocks. In general terms it may be said that most of the mucous surfaces to which air has free access may show smallpox lesions. The nasal, lingual, buccal, and pharyngeal surfaces commonly show an abundance of lesions. The œsophagus often contains pocks, but seldom in its lower third. At autopsy these lesions often appear as slightly excavated ulcers, frequently with attached blood clots.

Although a few of the older writers have described pocks in the *stomach* and *intestines*, it is extremely doubtful whether they occur in these regions. We have, in a number of instances, seen small, punctate hemorrhages in the gastric mucosa, and in one case a small, superficial ulcer, but never any genuine variolous lesions. A catarrhal condition of the gastric and intestinal mucous membrane is not rare. Follicular ulcerations in the intestines have doubtless been mistaken by some observers for smallpox lesions.

About the anus and a little higher in the rectum the remains of pustules are said to be occasionally observed. This must, however, be rare, as Perkins and Pay in forty carefully performed autopsies failed to find any pocks in these regions. The bladder and urethra are always free of lesions, with the exception of the meatus urinarius.

Councilman, Magrath, and Brinckerhoff, from a careful study of the various membranes in smallpox, conclude that "the lesions of the mucous membranes are in degree proportional to the extent and to the severity of those of the skin. At an early stage of development they resemble the lesions of the skin, but owing to the structure of the mucous membrane the resemblance is lost in the course of their evolution. In the absence of a restraining horny layer, the degenerated epithelial cells are cast off and the vesicle within the epidermis is rarely seen, the pustule never."

The *respiratory tract* is more attacked than any of the internal surfaces. The larynx, as is known, is often severely involved. Pustules and ulcers are often found in the trachea, particularly at the division of the bronchi. They may, moreover, be encountered in the bronchial tubes of the third and fourth order. The small bronchi often exhibit in addition a catarrhal process, with necrosis of the surface epithelium and fibrinous or purulent inflammation. The lungs not infrequently show small areas of catarrhal pneumonia.

Curschmann aptly says that "true pocks on *serous membranes* are fables belonging to antiquity, but congestion, inflammation, and ecchymoses are common."

The meninges and the peritoneum seldom exhibit pathological changes, but the pleural surfaces are not infrequently inflamed.

Stokes¹ in one case found the pleural surfaces dotted with abundant vesicles about the size of number six shot. On microscopic exami-

¹ Loc. cit.

nation they appeared to be large lymph spaces distended with serous fluid.

The solid *abdominal viscera* undergo serious alteration of structure. The *liver* in fatal cases of smallpox is nearly always enlarged, the increase in size in some cases being most pronounced. The surface of the organ and the hepatic tissue upon incision exhibit a coloration much paler than normal. Nearly all writers refer to degenerative changes in the liver varying from cloudy swelling to a more or less intense fatty degeneration. Weigert describes areas of local coagulation necrosis in which are seen nuclear detritus and many degenerated cells without nuclei. Siderey says there is intense congestion with migration of white blood corpuscles and swelling of the endothelial lining of the capillaries; later the liver cells swell and undergo fatty degeneration.

Roger and Garnier¹ made a microscopic study of the liver in seventeen smallpox cases. They conclude that variolous hepatitis is usually total and may affect the interstitial or parenchymatous tissue. Fatty hepatitis is said to be the most common, having been found in six out of eleven cases of coherent or confluent smallpox. In hemorrhagic smallpox, it is, according to these investigators, constant. Necrotic hepatitis is more rare and is characterized by cellular necrosis in limited foci or diffuse bands. This condition was observed alone in two cases, and in two others associated with fatty degeneration. A third variety, hemorrhagic hepatitis, was found in one case in a child with congenital variola.

Ponfick and Curschmann both state that in purpura variolosa the liver is normal in size and color and does not exhibit the degenerations above referred to.

According to Ponfick,² the *spleen* in those who die early is swollen, soft, and of a light-red color. It later resumes its normal appearance except in purpura variolosa, in which variety it is small, hard, and dark red, with prominent follicles.

Roger and Weill³ found the spleen hypertrophied in every one of sixteen fatal cases of confluent smallpox. Among twelve hemorrhagic cases it was enlarged in four instances. The most interesting microscopic changes are the presence of nucleated red blood corpuscles, and a predominance of mononuclear leukocytes among the white cells.

Perkins and Pay⁴ noted hemorrhages into the splenic pulp in six out of forty autopsies; three of these were cases of purpura variolosa.

The *kidneys*, like the liver, show changes varying from cloudy swelling to fatty degeneration. Arnaud⁵ made histological examinations of the kidneys in thirteen cases of smallpox. The changes were briefly of two types—an interstitial cell infiltration and lesions of the epithelium of the tubules.

Stokes⁶ has recently made a careful study of the kidneys in variola.

¹ Étude anatom. et chim. du foie dans la variole, Archiv. de méd. exper., September, 1901.

² Ueber die Anat. Veränderungen der Innern Organen bei hemor. u. pust. Variola, Berl. klin. Woch., 1872, No. 42.

³ Les maladies infectieuses, Paris, 1902.

⁴ The Etiology and Pathology of Variola, Journal of Medical Research, October, 1903.

⁵ Revue de méd., 1898, tome xviii. p. 392.

⁶ Loc. cit.

Extensive changes were found in every kidney examined. In one case an acute interstitial nephritis such as described by Councilman in diphtheria and scarlet fever was found. In one very malignant case the changes noted were as follows: In the glomeruli the capillaries contained clear hyaline material within the lumen. This was due to an actual degeneration of the endothelial lining of the glomerular capillaries. At times the hyaline material formed a large crescentic mass of homogeneous clear material in the capsular space. The epithelium of the convoluted tubules was swollen and the cytoplasm of the cells contained numerous granules. In many of the cells the cytoplasm had completely degenerated into a mass of clear droplets which produced hyaline casts in the lumina of the tubules. The clear droplets took Weigert's stain for fibrin. The *adrenal bodies* were found by Perkins and Pay¹ to frequently show well-marked fatty degeneration of the cells of the medulla.

The heart in fatal cases of confluent smallpox is usually relaxed, soft, and somewhat enlarged. Microscopically the changes are those of cloudy swelling and fatty degeneration; fragmentation of the muscle fibres is commonly seen.

In purpura-variolosa, according to Ponfick, the organ is firm, contracted, and of a brownish-red color.

The Lymphatic Glands.—Roger and Weill² state that hypertrophy of the glands in variola follows the same rule as splenic enlargement; it is very marked in the pustular variety and slight or absent in the hemorrhagic form. Microscopically the cells found are similar to those seen in variolous bone-marrow; neutrophile myelocytes are notably present and in addition there are some basophile myelocytes and occasionally eosinophiles. Giant cells are also seen, and in hemorrhagic smallpox nucleated red blood corpuscles.

Stokes examined the cervical and bronchial glands in smallpox and found extensive focal necrosis containing an abundance of streptococci.

Bone-marrow.—In 1873 Golgi³ made a study of the bone-marrow in ten cases of pustular and twenty-five cases of hemorrhagic smallpox. In the pustular form he found a great increase of the white cells, while in the hemorrhagic variety he found a great increase of nucleated red cells, a distinct diminution of the white cells, some of which were in process of fatty degeneration, and diffuse hemorrhages in the medullary spaces. The medullary tissue was red and almost as fluid as blood.

Chiari⁴ found a condition which he designated "osteomyelitis variolosa" in 72 per cent. of twenty-two cases examined. This process is characterized by pea-sized, whitish, grayish or yellowish nodules, widely disseminated in the marrow substance. These consist of epithelioid cells derived from proliferation of the marrow cells. An early necrosis

¹ Loc. cit.

² *Maladies Infectieuses*, p. 721.

³ *Sulle Alterazioni del Midollo del osso nel variola*, Rivista clinica di Bologna, 1873, p. 283.

⁴ *Osteomyelitis Variolosa*, Ziegler's Beiträge z. pathol. Anat. u. allg. Pathol., 1883, Bd. xiii., S. 13; and Zeitschrift f. Histologie, Bd. vii., S. 325.

sets in. Chiari regards these focal necroses as due to the specific variolous poison.

Courmont and Montagnard,¹ and Roger, Josué and Weill have studied this subject with results which are in accord with those above detailed.

Roger² says: "The cellular formula of bone-marrow in variola is as follows: Great predominance of mononuclear cells and relative diminution of polynuclears." The cellular findings are analogous to those of the blood. The marked differences noted by Golgi in the marrow of the pustular and hemorrhagic smallpox were not confirmed by these writers.

The Testicles.—The occasional occurrence of orchitis variolosa has led to a careful microscopic study of the structure of this organ after death.

Chiari found pathological changes in the testicle very frequently among the cases that came to autopsy. The specific variolous change is a focal necrosis similar to that observed in the liver, spleen, kidneys, and lymph glands by Weigert. The alteration begins early in the course of the disease, but reaches its height during the suppurative stage. The inflammatory foci are said to be located predominantly and primarily in the interstitial tissue, although Stokes,³ in a recent examination of two cases states that the process began as a necrosis of the epithelial cells of the seminiferous tubules.

In twenty-seven examinations of the testicles Perkins and Pay⁴ found well-marked necrosis in eight. Examination of the ovaries failed to discover any lesions of this character.

The *brain* and *spinal cord* ordinarily exhibit no structural alteration in smallpox, save at times a moderate amount of congestion and œdema. In a small proportion of cases grave changes may occur even in mild cases. To this attention has been called under the heading of Complications of the Nervous System.

Hemorrhagic Smallpox.—The pathological findings in *hemorrhagic* smallpox differ in many respects from those in ordinary cases.

The condition of the spleen, liver, and kidneys has already been referred to. It is uncommon to find hemorrhages in such viscera as the liver, kidneys, spleen, brain, etc. On the other hand, the bloody extravasations are very common upon the mucous and serous structures of the body. These are seen as ecchymoses of these surfaces and as free accumulations in the cavities. The pleural and pericardial sacs not infrequently contain bloody fluid or clots and less commonly the peritoneal cavity.

The loose tissue of the anterior and posterior mediastina and the retroperitoneal space often exhibit bloody exudates. Hemorrhage into the kidney structure itself is extremely rare, but it is seen in the renal pelvis and beneath the capsule of the kidney.

¹ La moelle osseuse dans la variole, XIII. International Medical Congress, Section on General Pathology, Paris, 1900.

² Les maladies infectieuses, p. 700.

³ Loc. cit.

⁴ Loc. cit.

Ecchymoses may occur in synovial membranes and free hemorrhage into the cavity of the joints. Zülzer, cited by Curschmann, speaks of the frequent occurrence of hemorrhages into the sheaths of nerves, but Wagner could not corroborate this observation.

As might be naturally expected from the symptomatology of hemorrhagic smallpox, practically all of the mucous membranes may be involved in the hemorrhagic process. Bleeding may occur from any portion of the alimentary canal, from the mouth to the anus; the same is true of any part of the respiratory mucous membrane, from the nostrils to the lungs; hemorrhagic infarcts may form in the pulmonary tissue.

Subconjunctival hemorrhage is frequent and constitutes a conspicuous and characteristic early symptom of purpura variolosa.

Bloody extravasation into the Fallopian tubes and uterus is extremely common. Hemorrhage into the structure of the testicles and ovaries is rarely seen, although the Graaffian follicles of the latter are said to be occasionally infiltrated with blood.

Councilman, Magrath, and Brinckerhoff¹ classify the changes occurring in the various organs and tissues in smallpox as follows:

A. Lesions in character and in distribution fundamentally specific and due to the presence of a parasite peculiar to the disease.

B. Lesions associated with the above, of indeterminate specificity, in kind analogous with those present in many of the infectious diseases, but in degree characteristic of variola.

C. Lesions caused by accessory etiological factors, bacteria whose presence and activity are conditioned by the specific infection.

Concerning the lesions in the two latter groups these writers summarize as follows:

1. Proliferation within the hæmatopoietic organs is constant and well marked, and gives rise in the spleen, the lymph nodes, and the bone-marrow to the formation of mononuclear, basophilic cells, and in the lymph nodes and the marrow to phagocytic endothelial cells. The former pass into the blood in large numbers. This process is present to some degree in other infectious diseases, but is here so prominent as to be well-nigh characteristic.

2. Cellular infiltration with the mononuclear basophilic elements above mentioned, focal and interstitial in distribution, occurs constantly in the testicle, and usually in the kidney, in the liver, and in the adrenal glands. In the testicle this infiltration, by pressure and by thrombosis, causes anæmic focal necrotic lesions, which seem to be specific of the disease.

3. Degeneration, focal in character, apparently not anæmic, but due to the action of toxins, and leading to necrosis, at times with hemorrhage and accompanied by focal formation of phagocytic cells, is present in the blood-forming cells of the bone-marrow, and constitutes a lesion almost pathognomonic, but devoid of parasites. Diffuse degeneration,

¹ Journal of Medical Research, February, 1904.

toxic in character, is present in the liver, the kidney, the adrenal gland, and the testicle; in the liver cloudy swelling is more marked than it is in any other acute infectious disease. Otherwise, the degeneration is not to be distinguished from that due to bacterial infection.

4. Inhibition of cell differentiation by the action of toxins is evidenced in the bone-marrow in the absence of complete transformation of antecedent cells into polynuclear leukocytes, and in the testicle in the absence of spermatogenesis. The first mentioned is a condition seemingly peculiar to variola.

5. The paucity of polynuclear leukocytes, alike in the specific lesions, in the focal degenerations, and in the bone-marrow, is a condition so common and so pronounced as to render it a striking peculiarity of the disease.

The toxins of extraneous bacterial infection may contribute to the production of acute parenchymatous degeneration of the liver, the kidney, the adrenal gland, and the testicle, which are already mentioned as associated lesions of the disease.

In addition, pyogenic bacteria may cause the formation of boils, cellulitis, abscesses, erysipelas, and gangrene.

The Blood. Red Cells.—The red blood corpuscles, according to Hayem,¹ undergo greater destruction in smallpox than in any other fever. This is not noted until after the permanent subsidence of the fever. The diminution in the number of the red cells is most pronounced in the hemorrhagic and confluent cases, in which one or two million erythrocytes per cubic millimetre may be lost in a very brief period. In hemorrhagic smallpox the anæmia comes on more rapidly; in a patient dying on the seventh day, Hayem counted but 2,000,000 corpuscles. There is likewise a reduction of the hæmoglobin, and this may be apparent before the cells are diminished in number. During the febrile period of the disease the red cells are normal or increased in number, perhaps due to concentration of the blood. Fibrin is increased after suppuration begins.

White Cells.—The examinations of the blood with reference to the leukocytosis have not given entirely uniform results in the hands of different investigators.

In 1870 Brouardel described the existence of a leukocytosis in the pre-eruptive stage of the disease which increased during the development of the eruption and diminished after the occurrence of pustulation. In the very mild and in the very malignant cases the leukocytosis was in abeyance.

Verstraeten, in 1875, stated that the leukocytosis was proportionate to the severity of the disease, and was, therefore, most marked in hemorrhagic smallpox, a remark that has not been verified by more recent investigators.

Hayem, Halla, and Pée, each showed that there is a leukocytosis more or less pronounced in all forms of the disease.

¹ Du sang et de ses altérations anatomiques, Paris, 1899.

A valuable contribution to our knowledge of the subject was made by Pick¹ in 1893. Forty-two cases representing all grades of severity were examined. He demonstrated more or less leukocytosis in all but the mildest cases. In mild cases the leukocytosis is slight, not often exceeding the high normal limit. In severe cases it is demonstrable only after the vesicular stage is reached, and attains its maximum about the ninth to the eleventh day, then slowly subsiding unless interrupted by complications. In confluent and hemorrhagic cases the leukocytosis according to Pick is insignificant and attributable to the occurrence of suppuration or complications.

Weil² examined the blood of twenty-four cases of smallpox of various forms at intervals of a few days.

Courmont and Montagnard³ studied twenty cases of smallpox, examining the blood for the most part daily. The conclusions of Weil and Courmont and Montagnard differ only in detail and are herewith submitted as summarized by Ferguson:⁴

Variola is (1) always accompanied by a leukocytosis characterized by a notable increase in the mononuclear cells of small and medium size. (2) During the stage of vesiculation, pustulation, and desiccation alike, the polymorphonuclear leukocytes are proportionately reduced in numbers. (3) This special leukocytosis is accompanied rarely in slight cases, but regularly in graver cases, by the appearance in the blood of cellular types not normally found there, namely, (a) intermediate or transitional forms of the neutrophile cells; (b) mononuclear neutrophiles (myelocytes); (c) nucleated red blood corpuscles; (d) mononuclear eosinophiles; (e) very large giant forms of non-granular mononuclear cells; (f) plasma cells (Weil). (4) In hemorrhagic cases a leukocytosis, if present at all, only attains feeble proportions. (5) Cases terminating fatally are characterized by more or less abrupt fall in the number of leukocytes.

In Weil's cases the leukocytes varied in six cases from 6000 to 10,000; in thirteen cases from 6000 to 13,000; they exceeded 15,000 in nine cases, 20,000 in three cases, 25,000 in three cases, 30,000 in one case, and 35,000 in one case.

Ferguson⁵ in 1903 made a careful study of the blood of sixteen cases of smallpox. He states that his findings are substantially in accord with the results obtained by Weil and Courmont and Montagnard. He remarks "that the feature which characterizes the leukocytosis, in distinction from that which is found to accompany the majority of the acute exanthemata, is that it is mononuclear and not polymorphonuclear in character. In other words, the condition is one in which the smaller

¹ Untersuch. ueber das qualitativen Verhalten der Blutkör. bei Variola, etc., Arch. f. Derm. u. Syph. Vienna, 1893, Bd. cv. p. 63.

² Thèse de Paris, 1901, and Étude qualit. et quant. de la leucocytose variolique, Compt.-rend. Soc. de biol., Paris, June 23, 1901.

³ La leucocytose dans la variole, Compt.-rend. Soc. de biol., Paris, June 22, 1900, p. 568; *Ibid.*, June 30, 1900, Cong. internat. de méd., Paris, 1900, p. 184.

⁴ The Leukocytosis in Variola, Journal of Pathology and Bacteriology, 1906, vol. viii. p. 411.

⁵ *Loc. cit.*

mononuclear elements (including the lymphocytes) are increased at the expense of the polymorphonuclear elements.

The mononuclear leukocytes, in a series of eight mild and discrete cases, averaged nearly 50 per cent., and in some cases reached 66 per cent. of the total leukocytes. In more severe cases the mononuclears did not attain the level reached in the milder cases. In the most severe cases the relative and absolute increase of this variety was to a certain extent obscured by the presence in the blood of myelocytes in greater or less numbers—an occurrence which accentuated the reduction of the polynuclears.

The eosinophile cells, according to Ferguson, are increased both relatively and absolutely in the earlier stage of the illness, but undergo a distinct reduction at a later period. Eosinophiles of the mononuclear variety are very exceptionally seen and only in the most severe cases.

In severe cases they are found in the blood elements normally occurring in the bone-marrow in numbers which are not often realized in other acute infectious diseases.

Magrath, Brinckerhoff, and Bancroft¹ have recently studied the leukocyte changes in fifty cases of variola. In twelve of these serial observations were made. Four cases of purpura variolosa were included in the cases studied.

The authors find a greater or less degree of leukocytosis in all cases of variola. The typical case of severe variola vera which recovers without complications presents at the beginning of the eruption a normal or subnormal count, which increases with the development of the cutaneous lesions, then suffers a slight decline, rises again during the late stage of the eruption, and finally falls to normal during convalescence. Fatal cases often show a high leukocyte count in the early eruptive stage, but then a gradual fall until death. Mild cases may show no rise above the normal limits or a gradually increasing leukocytosis, reaching its acme after the lesions of the skin have passed their active stage.

The primary and secondary hemorrhagic forms of smallpox both show a marked hyperleukocytosis. The leukocyte picture in variola is characterized by an increase in the mononuclear cell types, although the minor variations in the leukocytic curves are dependent upon fluctuations in the absolute number of polymorphonuclear neutrophiles.

The leukocyte examination is considered to be of but little value in either diagnosis or prognosis.

Bodies in the Blood, and Infectiousness of the Blood.—A number of investigators have found motile bodies in the blood of persons and animals suffering from variola and vaccinia. Among these may be mentioned Doehle (1892), L. Pfeiffer (1893), Monti (1894), E. Pfeiffer (1895), Weber (1896), Walter Reed (1897), Huguenin (1897), Roger and Weill (1900), Dombrowski (1902), Roger (1902), and Magrath and Brinckerhoff (1904).

¹ The Leukocyte Reaction in Variola, *Journal of Medical Research*, February, 1904.

These bodies were at first thought to be peculiar to variola, but later investigations proved them to be present in other conditions.

Pfeiffer, Reed and Stokes, and Wegfarth point out that, while the granular cells described by them are most readily found in the blood during the progress of certain infectious processes, they must be regarded as normal constituents of the blood. In 1896, Müller, of Vienna, found constantly in freshly drawn blood of normal and diseased individuals "small, generally round, colorless granules" which are quite distinct from blood plates.

Magrath and Brinckerhoff¹ have recently investigated the infectiousness of the blood in smallpox. They conclude that bodies widely diverse in size and somewhat different in structure occur in the blood of patients with variola, and in that of the monkey inoculated with variola virus. They are somewhat more numerous during the secondary fever than at other times, and in severe than in light forms of the disease. Bodies of like sort are occasionally seen in the blood of healthy men, in that of the normal monkey, and were numerous in a case of malignant endocarditis. These bodies do not admit of positive identification with any known form of cytocytes variolæ. They may be accounted for as derivations or as degeneration products of blood corpuscles, as blood platelets, and in some instances as erythroblasts. The blood of smallpox patients inoculated upon the cornea of the rabbit does not produce a variolous keratitis.

THE BACTERIOLOGY OF SMALLPOX.

In the early part of the last century, Sacco (1809) found in vaccine lymph certain granules usually aggregated in masses and endowed with independent motion.² For over half a century no further investigations were made in this field. In 1863 Beale described in vaccine lymph very minute, transparent, hyaline particles which he regarded as the contagious principle of the disease.

Chauveau in 1868 added greatly to our knowledge of the nature of the vaccine lymph by demonstrating that the production of vaccinia depended upon the presence of its contained particles, for when these were removed the vaccine lesion could not be induced. He also showed that the activity of the virus was not interfered with by considerable dilution. Prof. Burdon-Sanderson, with improved technique, confirmed the work of Chauveau concerning the sterility of vaccine lymph freed of all solid particles.

Cohn in 1872 noted certain corpuscles in fresh vaccine lymph to which he gave the name *micrococcus vaccinae*. In 1873 Klebs isolated from vaccine virus micrococci growing in tetrads, to which he gave the name of *tetracoccus vaccinae*.

Koch (1882) and Cornil and Babes (1883) also noted the presence of

¹ Loc. cit.

² In the preparation of the historical aspect of the bacteriology of this subject the authors have made free use of the work of S. Monckton Copeman on Vaccination, London, 1899.

micrococci, the former in the vaccine vesicle of a child. Quist in 1883 grew micrococci on artificial media and, inoculating calves therewith, believed that in some cases he induced true vaccinia.

Voigt grew three species of bacteria on gelatin plates from vaccine lymph, and called one the vaccinococcus. This was found constantly, and grew in pairs and fours. Inoculations of calves were claimed to render them immune against subsequent vaccination.

Micrococci were isolated from vaccine lymph by Guttman (1886), Marotla (1886), Meguin (1886), Buist (1886), and Tenholt (1887).

In 1887 Hlava isolated from vaccine lesions the streptococcus pyogenes and various staphylococci. Garré in 1887 found in vaccine lymph two kinds of bacilli and a coccus which he regarded as specific. The coccus when inoculated upon calves was said to produce vaccine vesicles followed by immunity.

In 1887 Pfeiffer isolated from vaccine lymph a variety of bacteria, including a yeast, two sarcinæ, a short bacillus allied to proteus vulgaris, and certain micrococci. He expressed the belief that the causative agent would be found to belong to the sporozoa and not to the bacteria.

In 1889 Grigorieu described a micrococcus vaccinæ which produced a papular eruption in calves and conferred subsequent immunity against vaccination.

In 1890 Voitow isolated four staphylococci—*aureus*, *citreus*, *cereus*, and *albus*. He mixed cultures of these and claimed therewith to produce typical vaccinia in the calf.

Leoni in 1890 and Protopopoff in the same year found the staphylococcus pyogenes albus and micrococci.

In 1891 Copeman isolated from vaccine virus the yellow, white, and orange staphylococci. None of these microbes were regarded as the causative agent. Klein, in addition, found the streptococcus of erysipelas in human vaccine, the use of which was supposed to have occasioned an attack of this affection.

In 1891 Crookshank isolated by means of plate cultures a large number of bacteria, including micrococci, bacilli, torulæ, etc. He recognized these as well-known saprophytic organisms and regarded none of them as specific.

Besser in 1893 cultured the lesions of smallpox on the fifth day and obtained a growth of a small bacillus which he regarded as the cause of the disease.

In 1893, Straus, Chambon, and Ménard obtained numerous colonies of micrococci when gelatin plates were inoculated with fresh vaccine lymph, with or without glycerin. It was found, however, that when the glycerinated lymph was kept for a considerable period the number of colonies was greatly lessened.

In 1893 Anthony found four kinds of micrococci and several species of bacilli in different specimens of vaccine lymph. The micrococci included the staphylococcus pyogenes aureus, a grayish-white micrococcus which liquefied gelatin, a yellow micrococcus which did not liquefy gelatin, and an organism designated the "porcelain micrococcus,"

which was invariably present in fresh vaccine lymph. The bacilli found were the *bacillus subtilis*, the *bacillus mesentericus*, fluorescing bacillus, and a motile bacillus growing in yellow colonies; all of the organisms referred to were regarded as impurities save the "porcelain micrococcus."

Maljean in 1893 noted the presence in vaccine lymph of several micrococci, including a peculiar coccus producing brilliant-white colonies on different media. This "*coccus vaccinae*" grew as isolated points, as diplococci, and in short chains. It gave rise in calves to typical vaccine lesions. Subsequent observers failed to confirm the above claims.

Klein¹ described an extremely minute bacillus occurring during the early development of vaccine and variolous lesions. It was found in smallpox virus during the third or fourth day and in calf lymph seventy-two to ninety-six hours after vaccination. Clear lymph, collected aseptically, was spread on a cover-glass, heated, treated with 30 per cent. acetic acid for some minutes, and then subjected to prolonged staining in alcoholic gentian violet. Bacilli were present in abundance in the calf lymph and to a less extent in variolous material. Lymph from lesions five or six days old showed no bacilli or only a few here and there. Spore-like bodies were demonstrated in a few of the bacilli. It was found impossible to grow these organisms upon any of the ordinary media.

In 1894 Baillard and Anthony published the result of their work on the effect of glycerination of vaccine lymph upon the number of contained bacteria. Baillard found a white staphylococcus, a yellow staphylococcus, and the *bacillus subtilis* quite uniformly present in lymph. He concluded from his experiments that glycerination considerably diminished the number of bacteria, but did not destroy all. The *bacillus subtilis* and the *staphylococcus albus* were still living after a period of seven months.

Leoni, in 1894, working along similar lines, found that the germs usually present in vaccine lymph were destroyed by the glycerin in from one to four months.

In 1895, Landmann, prompted by the prevalence of excessively sore arms among children in Germany, investigated the bacterial content of the lymphs distributed from thirteen German institutes. He found that the number of germs in the different lymphs varied from 50 to no less than 2,500,000 per cubic centimetre. Among the microbes isolated were the *streptococcus pyogenes*, the *staphylococcus albus*, and the *staphylococcus aureus*.

Dr. Stephen C. Martin and Prof. Ernst, of Boston, in 1895, isolated a bacillus from vaccine lymph which they regarded as the cause of the disease. The bacillus was short and thin and grew only on ox or horse serum. The growth was of a white color; the organisms formed chains and, under certain circumstances, appeared as a micrococcus. With the fourteenth generation of this microbe a vaccine vesicle was produced on the arm of an infant in one attempt out of ten; better success was attained with inoculation of calves.

¹ Report of the Medical Officer to the Local Government Board, for 1892-93.

In 1895 Le Dantec found in vaccine lymph staphylococci related to the ordinary pus organisms. Those isolated from calf lymph had different characteristics from those obtained from human lymph; the former liquefied blood serum, while the latter did not.

In 1896, Arloing, after failing to establish the specificity of the organisms found in the vaccine lymph, concluded that the virulent agent of vaccinia must be a soluble toxin. From experimentally induced horsepox he isolated, with great care, a micrococcus which failed to produce vaccinia in the human subject and was also without immunizing effect.

Boureau and Chaumier, in 1896, in an examination of vaccine lymph, found a variety of microbes, including the staphylococcus aureus, cereus, and albus, micrococcus flavus, bacillus subtilis, bacillus luteus, bacterium termo, proteus vulgaris, a cladothrix, a fluorescing bacillus, and several other unidentified bacilli. These observers gave expression to the extraordinary opinion that the activity of the lymph was related to the presence of the staphylococci.

In reply to this contention Ménard in the same year again emphasized the statement made by Copeman, and by Straus and himself, that the microbes that can be isolated from the lymph are in no way essential to its specific action, and that its potency may be perfectly preserved, even though the micrococci are completely destroyed by glycerination.

Sacquépée in 1896 found in various specimens of vaccine lymph three species of staphylococci, the bacillus subtilis, the bacillus mesentericus, and an unidentified bacillus. The presence of the bacilli was considered to be due to accidental contamination.

Delobel and Cozette (1896-97), in collaboration with Gourny, concluded that the organisms most constantly found in vaccine lymph were a yellow and a white micrococcus. The bacillus subtilis and the bacillus mesentericus were often found when adequate care was not taken in the collection of the lymph.

Paul in 1896 made an extensive investigation of the bacteria occurring in vaccine lymph. He emphasizes the fact that the staphylococcus pyogenes aureus is, of all microbes, the most common resident of the lymph. Different samples of the lymph contained golden staphylococci which varied greatly in resisting power and virulence. While the use of a lymph containing an abundance of staphylococci should be avoided, yet the employment of such lymph is not necessarily accompanied by suppuration.

In 1897 Copeman and Blaxall carried out an exhaustive series of investigations on the bacterial flora of calf lymph, which led to a confirmation of views previously expressed, that calf lymph (or rather vesicle pulp) contains a large number of micro-organisms which are in no way related to its specific activity. Human lymph, on the other hand, was usually found to contain remarkably few microbes; this might have been due to the fact that the vesicle pulp was not removed in the latter, as in the case of calf lymph. Calf lymph carelessly collected was often contaminated with numerous saprophytes common to dust, in addition to certain pathogenic organisms.

SMALLPOX

A large number of specimens of lymph showed one or more of the organisms. The appended list shows the germs in the order of frequency and predominance.

1. *Coccus cereus flavus*; *staphylococcus cereus albus* (Basset).
2. Light, orange colored; small yeast, light-brown color; small non color, and growing very slowly.
3. *Coccus pyogenes albus* (Rosenbach).
4. *Coccus pyogenes aureus* (Rosenbach).
5. *Coccus pyogenes citreus* (Basset).
6. *Bacillus mesentericus vulgatus*.
7. *Bacillus subtilis*.
8. *Penicillia*, *mucors*, *aspergilli*: *sarcinae*—*lutea*, *aurantiaca*.

Members of groups one and two were always present. *Staphylococcus* was frequently present and the golden *coccus*.

1. The bacillus *subtilis* and *mesentericus* were accidental.
2. The former rarely occurred if the skin was cleansed before the lymph collected carefully.

These examinations were made of lesions produced by calf-to-calf vaccination. When one-month-old glycerinated lymph is used on man, remarkably few colonies of extraneous germs are found in the lymph produced.

If a drop of fluid be removed from an early vaccine vesicle of a healthy infant or calf under aseptic precautions, it will often be found to be sterile as far as any organisms cultivable upon ordinary media are concerned. Such lymph, nevertheless, will give rise to typical vaccine lesions when inoculated upon a susceptible individual.

Copeman and Blaxall state that the presence of pyogenic organisms in vaccine lymph does not in any way imply that the lymph is purulent and that inoculation of the same would lead to suppuration. A Berlin Commission reports that of eighteen samples of lymph examined, but five contained staphylococci which were pathogenic for small animals. It is important to note that these five specimens were used without harm in the vaccination of children. The streptococcus *pyogenes* was not found once by the Berlin Commissioners in sixty samples of lymph. It is not so uncommonly found in human lymph.

Copeman and Klein, in 1894, concurrently, though independently, described a minute bacillus in practically pure culture in specially stained preparations of vaccine lymph taken before the full maturity of the vesicles. These bacilli were either absent or present in scant number in mature lymph; it is suggested that in the latter stages they have given place to spore formation.

No growth was obtained upon the ordinary nutrient media. Later Copeman obtained pure cultures of this organism by inoculating the centre of hens' eggs with variolous crusts rubbed up with sterile water. The eggs were incubated for one month at 37° C. At the end of this time the ordinary egg contents were replaced by a creamy material which, examined on cover-glasses, appeared to contain a pure culture of the small bacillus. Inoculation of calves with this material produced

vaccine lesions, the lymph of which gave typical vesicles when transferred to children.

Copeman admits that the results of these interesting experiments are rendered inconclusive by the fact that the calves employed were inoculated elsewhere upon the body with ordinary vaccine lymph; every precaution, however, was taken to prevent contamination of the defined area inoculated with the egg culture. In later experiments Copeman and Blaxall succeeded in growing the small bacillus on other culture media.

In 1900 Nakanishi¹ isolated a bacillus from human and bovine vaccine lymph to which he gave the name of "*bacillus variabilis lymphæ vaccinalis*." This organism belongs to the pseudodiphtheria group and exhibits great variations in size and form. Inoculation of the cornea of rabbits with cultures of this bacillus produced bodies in the epithelial cells which were said to closely resemble the cytorrhyses variolæ of Guarnieri.

In the same year Levy and Finkler² independently described a bacillus found in vaccine lymph which they designated "*corynebacterium lymphæ vaccinalis*." This organism belongs to the pseudodiphtheria class and is probably identical with that described by Nakanishi.

Cause of Pustulation in Smallpox.—It is quite definitely established that the suppuration of the variolous pock is the result of the causative agent of the disease and is not due to secondary infection with pyogenic organisms. In the vesicular and even in the early pustular stage of the eruption the lesions will commonly be found to contain no bacteria cultivable upon ordinary media. In an investigation of the contents of smallpox vesicles and pustules³ we found 33 out of 34 cultures of lesions before the seventh day sterile. Frequently a drop of pus from a lesion was placed upon a nutrient medium and incubated without any visible growth developing whatsoever. In all, cultures were made from 82 lesions in 51 cases of smallpox; of this number 64 cultures remained absolutely sterile.

This work is in accord with most of the investigations upon this subject.

Perkins and Pay⁴ made 30 cultures from typical variola lesions at all of the various stages from the beginning vesicle to the full development of the ripe pustule. These were all negative with the exception of 4—1 on the eighth day, 1 on the ninth, and 2 on the tenth days of the eruption.

After the seventh or eighth day of the eruption various bacteria, chiefly streptococci, may be found in the lesions.

The Streptococcus Pyogenes in Smallpox.—The streptococcus is commonly found in the late pustules of smallpox and in many of the cutaneous complications, such as boils, impetigo, abscesses, erysipelas, gangrene, etc.

¹ Centralbl. f. Bakt. u. Parasit., 1900, Bd. xxvii.

² Deutsche med. Woch., June 28, 1900.

³ A Preliminary Study of the Contents of Variolous Vesicles and Pustules, Journal of the American Medical Association, 1903.

⁴ Journal of Medical Research, October, 1902.

After death streptococci are found in the cutaneous lesions and in the blood and internal organs in nearly all cases. There would appear to be in many cases an agonal or post-mortem diffusion of streptococci throughout the tissues. In 40 autopsies on smallpox patients made by Perkins and Pay streptococci were found distributed throughout the body of 38.

Ewing¹ found streptococci present in about 90 per cent. of the skin lesions cultured at autopsy. He also noted the presence of streptococci in the blood after death in every one of 29 cases examined. In 10 cases of varying severity in which the blood was cultured during life the results were negative.

Arnaud² found streptococci in the blood during life in 2 cases of hemorrhagic smallpox.

Perkins and Pay³ examined the blood in 20 cases of smallpox and found streptococci in 11 cases, before or just after death.

Omitting the varioloids and convalescents and considering only the more serious cases, a total of 16, with streptococci in 11, or 69 per cent.

It is evident from the above investigations that the streptococcus is almost constantly found in fatal cases of smallpox. While no one can seriously entertain the idea that its role in smallpox is causal, it is so uniformly present that some writers believe it bears a peculiar relation to the disease differing from most secondary infections. It should be remembered, however, that the same statement might be made with equal force in referring to the relationship between the streptococcus and scarlet fever.

Many writers regard the streptococcic bacteriæmia as the most frequent cause of death in smallpox. Councilman⁴ says: "As the result of the study of the disease, both by culture of the lesions and organs and by microscopic examination of tissues, we are inclined to regard bacterial infection as a more important agent in bringing about a fatal termination than the specific parasite. . . . The bacteria are chiefly streptococci."

Perkins and Pay, and likewise Councilman, suggest that the streptococci gain entrance to the circulation through the bronchial and pulmonary mucous membranes.

Perkins and Pay found that the pathogenicity of the streptococci isolated was markedly different. Some of the strains killed rabbits in two or three days, while others were without effect. The writers suggest that the failure of antistreptococcus serum prepared from one variety of streptococcus may be thus accounted for.

Protozoa in Variola and Vaccinia.—Grünhagen⁵ in 1872 appears to have been the first to call attention to the presence of protozoa in variola and vaccinia. He described in vaccine lymph, clear, refractive, sharply contoured bodies both free and attached to leukocytes.

¹ Proceedings of the New York Pathological Society, May, 1902.

² Rev. de méd., 1900, p. 303.

³ Journal of Medical Research, February, 1904, p. 358.

⁴ Loc. cit.

⁵ Bemerkungen Ueber den Infektionsstoff der Vaccin Lymph, Arch. f. Dermat. u. Syph., 1872, p. 150.

Renault in 1881 described peculiar bodies which he believed to be parasites in the epithelial cells of variola and vaccinia.

In 1887 Van der Loeff¹ found in a hanging drop of clear vaccine lymph numerous small, round bodies endowed with amoeboid movement; later he discovered the same bodies in smallpox pustules.

L. Pfeiffer published a series of papers beginning in 1887, describing the presence in variolous and vaccine lymph of the "monocystis epithelialis," a small, unicellular, rounded body which he regarded as the specific cause of smallpox. These bodies were also found in the epithelial cells of the Malpighian layer and were said to multiply by division and by endogenous spore formation.

In 1892 Guarnieri² made a most important contribution to the study of protozoa in variolous affections. He found in the epithelial cells of the skin in smallpox and vaccine vesicles, and in the cells of the cornea inoculated with variolous and vaccine virus, certain bodies which he designated the "cytoryctes variolæ" and the "cytoryctes vaccinae" respectively. (The name has reference to the alleged devouring of epithelial cells by the parasite and to the formation of a clear space about it.)

Guarnieri attempted the cultivation of these protozoa by inoculating the cornea of rabbits and guinea-pigs. At the end of fifty hours the cornea was scraped and the material examined in aqueous humor in a hanging drop. Small, refractile bodies were found which possessed amoeboid movements. Upon section of the cornea, bodies varying in size and shape were found in the deeper layers. Multiplication was said to take place by binary division and by gymnosporic formation. Bodies exhibiting a mulberry form were described.

Monti confirmed Guarnieri's findings and produced specific lesions in the cornea by inoculation with various tissues from cases of smallpox.

Ruffer and Plummer³ in 1894 described the parasite as a small, round body, about four times the size of a staphylococcus, lying generally in a clear vacuole in the protoplasm of the epithelial cells.

Guarnieri's work has since been confirmed by a number of investigators, including Jackson Clark (1894), von Sicherer (1895), Ernst Pfeiffer, Gorini, Lebrede, and Wasielewski.⁴

Wasielewski inoculated corneas with sterile substances and various bacteria and yeasts and failed to produce the typical inclusions seen when variolous or vaccine material was employed. He carried the latter inoculations from eye to eye for a number of generations and produced uniform lesions. From the thirty-sixth generation material was taken from the cornea and seven children vaccinated; of this number six out of the seven developed typical vaccine lesions.

Ferroni and Massari⁵ inoculated the cornea of rabbits and guinea-pigs with croton oil and India-ink and claim to have produced in the epithelial

¹ *Monatsh. f. prakt. Dermat.*, 1887, No. 5, Bd. vi. p. 189.

² *Centralbl. f. Bakt.*, August 25, 1894.

³ *British Medical Journal*, June 30, 1894.

⁴ *Centralbl. f. Bakt.*, 1897, Bd. xxi. p. 901; and *Zelt. f. Hygiene*, 1901, Bd. xxxviii. p. 212.

⁵ *La Riforma Med.*, 1894.

cells numerous small bodies apparently identical with those described by Guarnieri. They believe that the so-called parasites are in reality derived from the nuclei of epithelial cells and from leukocytes.

Salmon,¹ after a careful study of the staining reactions of the bodies described, likewise opposes the views of Guarnieri. He says: "The pseudoparasite is not an endogenous formation; it, therefore, of necessity has an extracellular origin, and the little mass of chromatin can have but one origin, namely, the migratory cells." Copeman² remarks: "No one can fail to be struck with the truth and completeness of Salmon's explanation of the facts previously observed."

An important article in opposition to Guarnieri's conclusions was contributed by Hückel³ in 1898. This investigator concedes the specificity, indolability, and immunizing properties of the lesions, but does not regard the bodies described as parasites. After a painstaking study he regards the inclusions as specific degenerative changes in the epithelial cells induced by the vaccine and variolous virus.

Councilman,⁴ basing his opinion upon his own extended investigations and those of his associates, regards the "cytocytes variolæ" as the parasite causing smallpox. The bodies occur within the epithelial cells, within the nuclei, and free. They do not occur as isolated structures, but follow each other in a cycle corresponding with the cycle of development of living things. In the different cases the same forms are found at the same period of the disease. The bodies increase rapidly in the lesions, and the lesions increase in extent by continuous infection of adjoining cells.

Councilman states that in vaccinia the same forms of parasites are found as in the cytoplasmic cycle of variola. The intranuclear forms, however, have never been seen in vaccinia. There is some difference in vaccinia in the size and in the rapidity of development of the parasites in the different tissues and in the different animals. "The differences are not greater than will be shown by the same flowers in different gardens."

Councilman and Tyzzer both discuss the dissenting opinions as to the parasitic nature of Guarnieri's bodies. Their derivation from leukocytes, red blood cells, extruded nuclear material, and specific cell degeneration is considered and the negative evidence presented.

Councilman says that bodies simulating those which occur in smallpox may be found as accidental products in a number of conditions. In these there is no complexity of structure, such as is found in most of the smallpox bodies, and there is no sequence representing growth development. The morphological products of cytoplasmic degeneration do not simulate the parasites. The cells in which the youngest forms of parasites are found have morphologically normal nuclei and cytoplasm. Moreover, the earliest degeneration in smallpox is found in the more superficial cells of the epidermis, while the parasites are in the lower.

¹ Ann. of Pasteur Inst., April, 1897.

² Vaccination, 1899, p. 123.

³ Die Vaccine Körperchen, Beitr. z. path. Anat., Bd. xxv., supplement.

⁴ Journal of Medical Research, February, 1904.

The intranuclear parasites are less apt to be confused with accidental products than are the cytoplasmic. They are found in nuclei in which there is no change in the chromatin and they stand in no relation to the chromatin.

The work of Councilman and his associates leads him to say: "We believe that these bodies in vaccinia and in variola are living things. We see no possibility of another conclusion. . . . We have constantly found the organism in connection with the developing lesions of the disease. . . . The bodies increase in size, and with growth details of structure appear which are always repeated, and for which the time relation, as far as can be determined, is the same. At the end of growth a form of multiplication takes place. Amœboid motion has been made out in the vaccine parasites by so competent an observer as Wasielewski, but although believing that the bodies are parasites, he very properly does not regard this as proof. . . . This view that the cytoryctes variolæ is the cause of variola must for the present rest on the fact that it is always associated with the lesions of the disease, develops further as the lesions develop, and is found under no other conditions."

Calkins¹ describes the life cycle of the variola parasite as follows:

The first development of the germ in the host is unknown; it probably takes place in the seat of primary infection, forming an organism which reproduces by germs or "gemmules," the process being known as "multiplicative reproduction." The gemmules are probably carried in the blood to the skin, where the further development takes place. The gemmules become intracellular (cytoplasmic) amœboid organisms which give rise to similar gemmules. These germs penetrate the nuclear membrane and develop into gametocytes (?), one forming the supposed male gametes and the other the female. The gametes conjugate (?); the zygote thus formed develops into a comparatively large amœboid organism, in which the pansporoblasts originate. These pansporoblasts give rise to primary sporoblasts, the entire process taking place within the nucleus and corresponding to the so-called "propagative reproduction" of other sporozoa. The spores thus formed may in turn infect fresh nuclei and grow directly into new, secondary sporoblasts which give rise to similar spores, a true "schizogeny" and a second means of autoinfection by which the organism spreads throughout the nuclei and cells of the skin and possibly to many of the other organs of the body. These spores may finally transmit the disease to new hosts.

Professor Bosc,² of Montpellier, France, states that the parasite of variola is a protozoon which presents itself in two forms—one a cytoplasmic and the other an intranuclear form.

The bodies described agree in all essential features with those portrayed by Councilman and his associates.

¹ The Life Cycle of Cytoryctes Variolæ, Guarnieri, Journal of Medical Research, February, 1904.

² Ext. des comptes-rendus des séances de la Société de biologie, October 17, 24, 1903, etc.

In vaccinia Bosc finds parasites which are intraprotoplasmic and reproduce by direct division. Similar bodies were repeatedly found in the lesions of sheeppox. In the latter disease Bosc claims to find changes in the lungs and liver which he regards as carcinomatous. Indeed, variola, vaccinia, sheeppox, syphilis, and cancer are said by him to contain "parasitoid intraprotoplasmic bodies."

Calkins gives the following provisional classification of the cytoryctes variolæ and allied sporozoa:

Class. Sporozoa.

Subclass. Myxosporidia.

Subclass. Neosporidia.

Order. Microsporidia.

Tribe. Polysporogenea.

Family. Cytoryctidæ. The organism forms one pansporoblast which is without a membrane. Nuclei absent. (The nosematidæ and phlistophoridæ also belong to this tribe.)

Genus. Cytoryctes, the cause of variola.

The caryoryctes (the paramecium parasite) and the lymphosporidium (brook-trout parasite) also belong to this genus).

Magrath and Brinckerhoff¹ have made a careful microscopic study of nine lesions of inoculated smallpox in six monkeys. They conclude that certain structures identical in form and staining reactions with those in the lesions of smallpox in man are found within the epithelial cells of the skin. The forms develop in a cycle such as is described by Calkins. The developmental series corresponds with the evolution of the lesion. The complexity of the structure, the staining reactions, and the serial nature of the bodies preclude the possibility of their being "products of degeneration."

THE DIAGNOSIS OF SMALLPOX.

The detection of smallpox in its pustular stage, particularly in well-marked eruptions, is a facile matter even for the merest tyro in medicine. The picture of a profuse pustular variola can scarcely be mistaken for anything else.

It is especially the mild and modified forms of smallpox that present difficulties in diagnosis. The degree of protection in varioloid may be so great that the eruption may consist of but a few papules, or, indeed, the eruption may be absent altogether, constituting a variola sine exanthemate. The diagnosis in such cases would, of course, present perplexities. It is a matter of considerable importance to ascertain whether variola is prevailing in a community, and whether the patient has been exposed to the infection. The inability to obtain satisfactory testimony as to direct exposure should not be allowed to influence the diagnosis, as infection may take place in the most subtle manner and from unsuspected sources.

¹ On the Occurrence of Cytoryctes Variolæ, Guarneri, in the Skin of the Monkey Inoculated with Variola Virus, Journal of Medical Research, February, 1904.

The degree to which the patient is protected by vaccination or previous attack of smallpox should always be investigated. The presence of a comparatively recent vaccine scar, or pits of a former attack, would constitute strong presumptive evidence against the existence of smallpox in the individual.

As variola is communicable during the initial stage, an early diagnosis often becomes highly important. If, in a given case, it be found that the patient was seized with a chill or had repeated rigors, followed by a sudden rise of temperature to an unusually high degree, and that there is epigastric tenderness, irritability of the stomach, and severe pain in the lumbar region, variola should be strongly suspected. If, together with these symptoms, there can be obtained a history of exposure to the variolous infection, the diagnosis becomes comparatively easy. But in many cases of variola, and particularly of varioloid, the initial symptoms are so indefinite that a diagnosis is quite impossible until the characteristic eruption appears.

There is no one symptom of smallpox which is so characteristic that it may not be absent. Curschmann regards the hemorrhagic initial exanthem, situated principally in the triangles of the thighs, as pathognomonic, but this occurs in a very small percentage of cases. In making a diagnosis, the prevalence of an epidemic, the vaccine condition of the patient, the history of the disease, and the symptoms as they present themselves should all be carefully considered.

The initial illness of smallpox may be confounded with influenza, typhus or typhoid fever, meningitis, and acute gastritis.

La Grippe.—In severe cases of la grippe the disease may be ushered in with intense headache, fever, delirium, and violent pain in the back and limbs, symptoms which strongly suggest smallpox. The differential diagnosis between these affections would be impossible before the appearance of the eruption. Knowledge of the prevalence of the one or the other disease would be an aid in the diagnosis.

Typhus Fever.—The early symptoms of typhus fever may be quite indistinguishable from those of the initial stage of smallpox. The appearance of the eruption will usually establish the diagnosis. The eruption of typhus is at first macular, and is seldom present on the face; while that of the smallpox is papular, and begins usually upon the forehead.

Meningitis.—In both meningitis and variola, violent headache, delirium, and coma may develop. In the cerebrospinal form, purpuric symptoms are not uncommon, but retraction of the head and rigidity of the muscles of the neck, so commonly seen in this affection, are seldom encountered in smallpox.

Typhoid Fever.—It is surprising how many patients sent into the Philadelphia Municipal Hospital with smallpox have been treated, during the initial stage of the disease, as cases of typhoid fever. This is perhaps owing to the frequency of the latter disease in this city. In an ordinary case of enteric fever the insidious onset and the gradual rise of temperature will distinguish it from variola, in which the onset

is sudden with chilly sensations, fever often reaching 104° or 105° F., and commonly with severe headache, backache, and vomiting.

Acute Gastritis.—The error of confounding the early manifestations of variola with acute gastritis is at times made in cases in which the initial illness is characterized by severe and persistent vomiting, with pain in the pit of the stomach. Attention to the associated symptoms and the history of the case should enable one to arrive at a correct diagnosis.

The mistaking of the early lumbar pain for *lumbago* could only result from an insufficient examination of the patient. *Lumbago* is not attended with fever and the other constitutional disturbances that characterize the initial illness of smallpox.

Measles.—Measles may be confounded both with the morbilliform prodromal rash and with the beginning true eruption of variola. The prodromal rash is non-elevated, irregular in distribution, with predilection for the trunk and extremities, of evanescent duration (twenty-four to forty-eight hours), and usually appears upon the second day of the initial illness in those about to develop the eruption of varioloid. In measles catarrhal symptoms are present and the eruption is later in making its appearance.

That measles may bear a close resemblance to smallpox is evidenced by the fact that in epidemics of variola cases of measles are not infrequently sent to the smallpox hospitals under erroneous diagnosis. It is the confluent form of variola which, in the early eruptive stage, resembles measles most, for in this type of the disease the face is often considerably suffused. Standing at the foot of the patient's bed in such cases it is frequently impossible, from the appearance of the eruption on the face alone, to distinguish between the two diseases. Some cases of measles are accompanied by more papulation than others, particularly on the face and wrists, and these are the cases that most strikingly simulate smallpox.

The diagnosis can, in the vast majority of cases, be determined by attention to the following points:

The constitutional symptoms preceding the eruption in smallpox are usually more severe (temperature 104° to 105° F.) and are commonly, though not always, accompanied by pronounced backache. The temperature, moreover, falls a few days after the appearance of the eruption, while the fever in measles at this time continues high. The catarrhal symptoms affecting the eyes and the respiratory passages and the buccal eruption, which are so constant in measles, are absent in smallpox, at least during the prodromal stage. Close inspection of the mouth in smallpox may reveal the presence upon the soft palate of rounded, glistening, pinhead-sized, reddish elevations, but these differ considerably from the bluish spots on the buccal mucous membrane in measles. The eruption in measles consists of large maculopapules which are soft and velvety to the touch, while the papules of smallpox are smaller and have a firm and shotty feel. The sweep of an experienced hand over the skin will often suffice to differentiate the

two diseases. Where there is doubt, twenty-four hours' delay will dispel all uncertainty, for by this time the eruption of measles will have become flatter and more diffuse, and the papules of smallpox firmer and more distinctly elevated.

Scarlet Fever.—The peculiar distribution and fleeting character of the scarlatiniform prodromal rash will enable one to distinguish it from scarlet fever.

Scarlet fever may, however, be closely simulated by that form of hemorrhagic smallpox in which the entire cutaneous surface becomes the seat of a diffuse, dusky-red rash, especially well marked in the crural triangle. This form of purpura variolosa is, however, usually preceded by excruciating backache. If the patient be watched for a short time a few ill-defined vesicles will usually make their appearance. The development of hemorrhages would not in itself be conclusive, as these might occur in hemorrhagic scarlet fever, except that hemorrhage beneath the conjunctiva would rather indicate the existence of smallpox. The early occurrence of sore throat would point toward the scarlatinal nature of the disease.

Chickenpox.—Smallpox may be distinguished from chickenpox, the disease with which it is most often confounded, by attention to the following considerations:

1. **Initial Symptoms.**—Fever, headache, backache, chills, vertigo, nausea, vomiting, etc., precede by two or three days the outbreak of the variolous eruption. In exceptionally mild cases, however, these symptoms may be slight or absent. In chickenpox there is usually complete absence of illness preceding the eruption. In some cases, however, particularly in adults, we have occasionally noted a prodromal illness suggestive of but much milder than that observed in smallpox. In chickenpox the fever and the eruption usually appear simultaneously.

2. **General Symptoms.**—The constitutional symptoms are usually more severe in smallpox than in varicella, but it must be remembered that we may encounter mild cases of smallpox and severe cases of chickenpox.

3. **Distribution of Eruption.**—In smallpox the eruption involves with predilection the face, hands, and feet; upon the trunk the lesions are, as a rule, more sparse. In chickenpox, the eruption is almost invariably most profuse upon the trunk, more particularly upon the back. Smallpox prefers the exposed surfaces and chickenpox the covered.

It has been stated that chickenpox does not attack the palmar and plantar surfaces; this statement is fallacious, inasmuch as the palms and soles are every now and then attacked in well-marked cases. Of course, one never sees such a profusion of lesions on these surfaces as is seen in smallpox.

4. **Character of the Lesions.**—In smallpox the eruption begins as firm, "shotty" papules, which slowly increase in size and develop into vesicles and pustules. The vesicles are hard, moderately uniform in size, and often, although not invariably, show umbilication; they are multilocular and difficult to rupture with the finger-nail. Chickenpox

lesions begin as vesicles containing perfectly clear serum; they have a rather soft or velvety feel, are often unilocular, thin roofed, can be easily ruptured with the finger-nail, and vary greatly in size, some being as small as a millet seed and others as large or larger than a dime. They do not umbilicate, save by desiccation beginning on their centre. The early drying with the production of a depressed, blackish crust in the centre and irregular puckering of the pustule on the periphery is highly characteristic of chickenpox.

5. Manner of Eruption.—The smallpox eruption usually comes out in a single crop and the lesions remain quite uniform in character. (It should be remarked, however, that the eruption on the face is always a little in advance of the development elsewhere.) The chickenpox eruption comes out in crops on successive or alternate days, and the lesions may be seen in varying stages of development. The coexistence of recent tense vesicles, older puckered vesicopustules, and dried scabs is highly characteristic of varicella.

6. Course of Eruption.—Smallpox lesions undergo a gradual evolution from papule to crust in the course of ten to twelve days (in mild cases five to six days). Chickenpox lesions last from two to four days (rarely longer) and then crust. The severity of the eruption is no absolute guide in the differential diagnosis, as severe cases of varicella may look far more formidable than mild cases of smallpox. The crusts of smallpox are dense and compact, while those of chickenpox are thin and friable.

While each group of symptoms just enumerated is characteristic respectively of smallpox and chickenpox, and while there should be no difficulty in differentiating between the two diseases when either group is complete, yet it must be admitted that smallpox sometimes occurs in a form so atypical as to make it difficult to decide to which category the symptoms belong.

It may, however, be stated in a general way that a mildly febrile eruption appearing without prodromal symptoms, being distinctly vesicular from the beginning, and commencing to desiccate on the second or third day, should be regarded as chickenpox; and, on the other hand, an acute exanthem preceded by an initial stage of forty-eight hours, in which the temperature was distinctly elevated, beginning as papules and ending in vesicles or vesicopustules, even though the period of evolution be short, should be regarded as smallpox. At any rate, it would be advisable, for the safety of the public, to regard such a case as suspicious, and surround it with such precautionary measures as are best calculated to prevent the spread of infection.

Syphilis.—It may at first seem strange that syphilis and smallpox should ever be confounded. Upon reflection, however, it will be seen that the two diseases have many phenomena in common. They are both infectious diseases due, we may assume, to the invasion of the blood with a micro-organism. Each has a period of incubation at the end of which there develop certain general manifestations accompanied by an exanthem and an enanthem. The resemblance may be still

PLATE XXXV.



**Pustular Syphilide bearing a Strong Resemblance
to a Beginning Confluent Smallpox.**

(Courtesy of Dr M. B. Hartzell.)

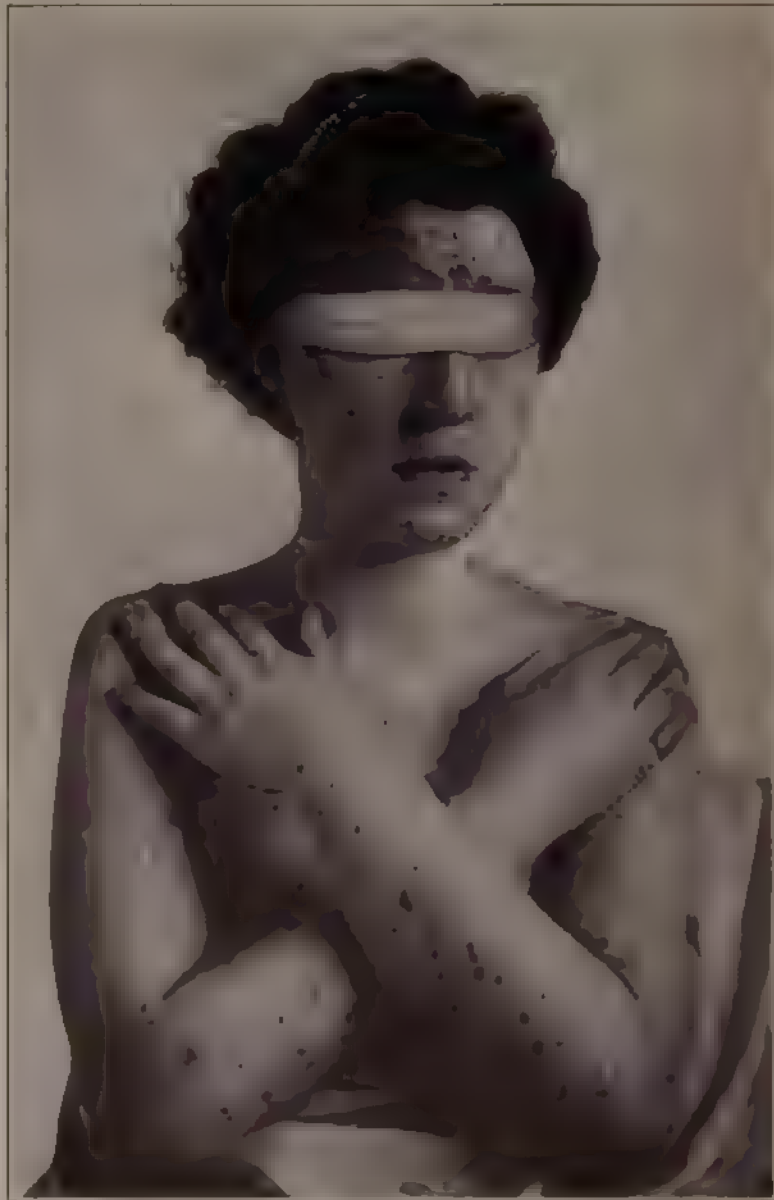
PLATE XXXVI.



Pustular Syphilide presenting a Resemblance
to Smallpox.



PLATE XXXVII.



Patient with a Variola-form Syphilide sent into the
Municipal Hospital as a Case of Smallpox.

further accentuated by the fact that the variolaform syphilide is not rarely associated with and even preceded by fever and general aches and pains.

It is particularly the pustular syphiloderm which is apt to be confounded with smallpox. The eruption at times may appear rather suddenly and pass through the stages of papule, vesicle, and pustule in a surprisingly brief period of time. The lesions may be quite firm to the touch and in other respects closely simulate those seen in smallpox.

In syphilis one can frequently obtain (1) *a history of infection* and a description of the initial lesion. Indeed, the chancre or its remains may still be detected. Not uncommonly there are present associated evidences of syphilis, such as mucous patches, flat condylomata, ulceration of the tonsils, alopecia, glandular enlargement, etc. The variolaform syphilide may develop after the disappearance of one of the earlier syphilitic eruptions.

2. *The onset of the two diseases* is, as a rule, quite different. The syphilitic subject will usually give a history of having felt weak and debilitated for some weeks. If fever precedes the eruption it is ordinarily not very high and is not accompanied by severe prostration. When the eruption appears the patient usually calls upon the physician at his office or at the hospital. We do not note that sudden illness which precedes unmodified smallpox. In the latter disease, two or three days before the efflorescence appears, the patient experiences a chill followed by a rise of temperature, often to 103°, 104°, or 105° F. There are severe headache, backache, vomiting or nausea, vertigo, general pains, and severe prostration. The patient, instead of calling upon the physician, sends for him.

It must be remembered, however, that in varioloid the initial symptoms may be mild or absent. On the other hand, in rare cases, syphilis may present an initial illness which strongly counterfeits that of smallpox.

3. *The development of the eruption* in smallpox is rather sudden. Ordinarily in twenty-four to forty-eight hours the full complement of lesions has appeared. In syphilis the eruption may continue to come out for quite a number of days in successive crops. It must be admitted, however, that in modified smallpox three or four days may sometimes elapse before the complete appearance of the exanthem.

4. *The distribution* of the variolaform syphilide may be identical with that observed in smallpox. Frequently, however, variations may be noted. The pustular syphilide may involve the trunk more copiously than the face; this would be exceedingly rare in well-marked smallpox. The dorsal surface of the wrists and hands are nearly always involved in smallpox, but may escape entirely in syphilis. The palms of the hands and soles of the feet are always involved in severe smallpox; in moderate eruptions they nearly always present some lesions, and in varioloid they may or may not escape completely. The pustular syphilide, on the contrary, attacks the palmar and plantar surfaces with the greatest rarity. The writers have observed in one case a single lesion

upon the palm of one hand, and in another instance a deep-seated pustule upon the lateral surface of the sole.

5. *The character of the eruption* in syphilis and smallpox may, in the beginning, be so nearly identical as to make a diagnosis from the eruption alone quite impossible. It will be noted, however, that the efflorescence of smallpox presents a much greater uniformity in the character and development of the lesions over the body than does syphilis. Syphilis is characterized by an essentially multiform eruption; it is not uncommon to find small pustules, large pustules, and papules interspersed, and these in varying stages of evolution and involution.

The vesicles and pustules of syphilis are usually conical and involve merely the summits of the elevations; they never become full and globular, and fill the entire lesion as do those of smallpox. Beneath the syphilitic crusts considerable ulceration not uncommonly occurs; according as this is slight or severe there will be seen upon detachment of the crusts, a small, reddish-brown pigmented stain or an excavated ulcer. The latter heals with the production of a depressed scar.

6. *The course of the syphilitic eruption* is relatively chronic compared with that of smallpox. The lesions of variola undergo a striking change in a few days. The syphilitic efflorescence is indolent, and presents, as a rule, no decided alteration of appearance within this period of time. By the sixth or seventh day in smallpox the lesions develop into those large, full, round, hemispherical pustules which are so characteristic of the disease.

Finally, to the physician who has seen much of smallpox, there is a something in the picture, an impression given by the *ensemble*, which, while not definable in language, is, nevertheless, of subtle aid in the diagnosis.

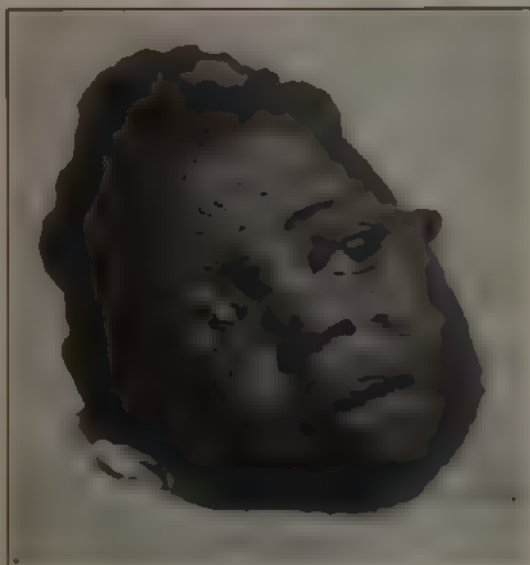
Roseola Vaccinosa.—Vaccination with animal virus sometimes causes an erythematous or rubeoloid rash, known as roseola vaccinosa, to appear from the eighth to the twelfth day of the vaccine disease. We have occasionally known this rash to have been mistaken for the eruption of variola, especially during epidemic visitations of the disease. The distinguishing features are that it accompanies vaccinia, that it is not preceded by a very high temperature, and that it consists of macules rather than papules.

Acne.—Mild cases of varioloid exhibiting but a few papulopustules about the face may bear a close resemblance to acne. The history of exposure, the existence of an initial stage, and the progressive evolution of the lesions will speak for the variolous nature of the eruption, while the presence of blackheads, a history of previous outbreaks in the individual, and the absence of preceding illness will decide in favor of acne.

Drug Eruptions.—Drug eruptions, particularly those resulting from the ingestion of the iodides and bromides, may simulate the exanthem of smallpox. The history and absence of an invasive stage will usually suffice to make the diagnosis clear.

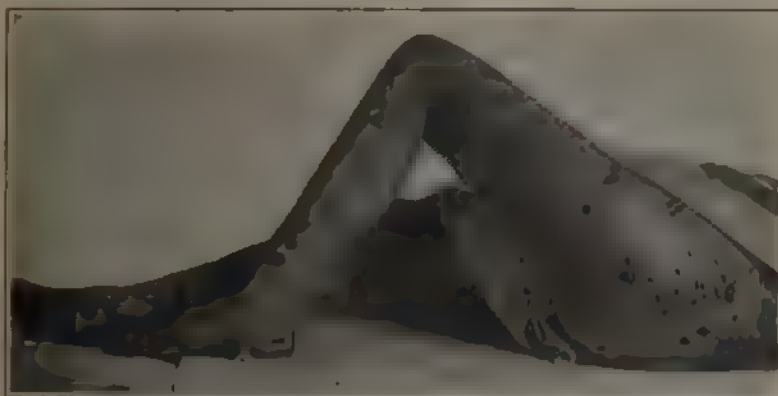
Impetigo Contagiosa.—A confounding of smallpox with impetigo contagiosa can come only from a misunderstanding of the nature of the latter disease, which is a purely local dermatosis resulting from inocula-

FIG. 48



Pustular bromide eruption, resembling smallpox in an infant suffering from tuberculous meningitis.

FIG. 49



Pustulobolous eruption, resulting from the ingestion of large doses of bromides, sent into the hospital as a case of smallpox.

tion of the skin with certain pyogenic micro-organisms. The eruption is usually limited to the face and neck, although occasionally a few lesions may be present upon the hands. The trunk and lower extremities are, save in rare cases, free of eruption. The lesions do not ordi-

narily exceed a dozen in number. They are usually discrete, thin-roofed vesicles and blebs, which rapidly become turbid and dry into yellowish, flat crusts. These are cast off, leaving faint, reddish stains. The vesicopustules are extremely superficial and flat, and appear to be on the skin rather than in it. The disease being local in character, there is, as a rule, neither fever nor any other systemic disturbance. The eruption is both contagious and autoinoculable, the infection occurring through direct or intermediate contact. The disease is more common in children than in adults.

Glanders.—Glanders in an early stage may be mistaken for smallpox. The febrile symptoms are not unlike those of variola, and the sub-epidermic abscesses when small feel like hard infiltrations in the skin.

FIG. 50



Papular bronchial eruption resembling smallpox in an infant suffering from tuberculous meningitis.

In this disease, however, there are, in addition, deep-seated abscesses, infiltration of the areolar tissue, rapid ulceration, and at times gangrene. The disease is rare, and the patients are usually stablemen.

Eczema.—Severe crusted eczemas of the face may bear a rough resemblance to confluent smallpox during the desiccative stage. We have known physicians experienced in smallpox to make this error through a hasty and superficial examination of the patient. Inspection of the trunk and extremities will make the diagnosis clear.

During epidemics the anticipatory attitude of the physician's mind will often lead him to suspect and diagnose as variola diseases which bear only a superficial or remote resemblance to it. Thus, patients with febrile herpes, herpes zoster, erythema multiforme, and other skin diseases have at such times been sent to smallpox hospitals as cases of

variola. Contrariwise, in the absence of an epidemic mild cases of smallpox are very likely to be overlooked.

Whenever the diagnosis between smallpox and a disease simulating it is in doubt, observation of the progress of the eruption for a period of twenty-four to thirty-six hours will usually make clear the nature of the disease.

THE PROGNOSIS OF SMALLPOX.

Since the introduction of vaccination the presence or absence of a typical vaccine scar on a patient is an important factor in the question of prognosis in smallpox. Formerly, smallpox was not only more common, but uniformly far more fatal, and therefore much more dreaded than at the present time.

During the last century but few diseases claimed a greater number of victims than variola, but at the present time, especially in countries where vaccination is carefully and systematically practised, the proportion of deaths from this malady is not greater than 0.7 per cent. of the entire mortality, and where revaccination at the proper age is also enforced, this proportion is even much less. In the prevaccination period one-tenth of all the children born died from smallpox; now the mortality from that disease among young children where vaccination is compulsory is almost *nil*. According to Juncker smallpox killed in the prevaccination days on an average 400,000 persons every year in Europe. In 1803 King Frederick William III., of Prussia, stated that the average yearly mortality rate from smallpox in Prussia was 40,000. In Prussia, where vaccination and revaccination are rigidly enforced at the present day, smallpox is almost unknown.

Age.—The age of the patient is of the greatest importance in considering the prognosis of smallpox. It is comparatively rare for an infant under one year of age to survive an attack of unmodified smallpox. So also at the other extreme of life the death rate is excessively high. In children of from one to five years of age the disease is also very fatal, but among those of from five to fifteen years the chances of recovery are rather better than in adult life.

SMALLPOX PATIENTS TREATED IN THE MUNICIPAL HOSPITAL, SHOWING MORTALITY ACCORDING TO AGE.

SERIES I.

Age.	Cases.	Died.	Percentage.
Under 1 year	60	37	61.66
1 to 15 years	530	187	35.28
15 " 25 "	1362	402	29.51
25 " 45 "	1215	365	30.04
45 years and upward	227	88	38.77
Total	3394	1079	31.79

SERIES II.

(Similar table with somewhat different age classification)

Age.	Cases.	Died	Percentage.
Under 1 year	57	29	50.87
1 to 5 years	159	50	31.45
5 " 10 "	180	20	15.38
10 " 15 "	66	8	12.12
15 " 25 "	371	55	14.82
25 years and upward	1096	172	15.69
Total	1879	334	17.80

The above tables give the smallpox mortality according to age, and include both the vaccinated and the unvaccinated cases. All of the patients under one year of age were unvaccinated except a few who were vaccinated after infection—i. e., during the incubation period. Likewise, practically all of the children under five years of age were unvaccinated.

In Series I. are included the statistics of the large and malignant epidemic of 1871-72, and of a subsequent severe epidemic; while in Series II. are included the statistics of the recent and much milder epidemic of 1901-02.

Race.—When smallpox prevails among aboriginal tribes the mortality is extremely high. It is commonly stated that the death rate of variola among negroes is much higher than among whites. This statement has scarcely been borne out by our experience. Negroes are extremely negligent as regards vaccination, and the number of unvaccinated blacks received in smallpox hospitals is apt to relatively exceed the number of unvaccinated whites. A truer comparison of mortality rates will be obtained, therefore, in contrasting the unvaccinated of both races.

In the tables here shown, the mortality rate among the negroes is somewhat higher than among the whites, although the difference is not great:

NEGROES AND WHITES ADMITTED TO MUNICIPAL HOSPITAL.

	Cases.	Deaths.	Percentage.
White	6181	1530	24.95
Black	1073	407	38.79
Total	7254	1937	26.89

UNVACCINATED NEGROES AND WHITES.

	Cases.	Deaths.	Percentage.
White	2036	910	44.69
Black	687	315	45.85
Total	2723	1225	45.33

Sex.—Sex influences prognosis to little or no extent.

Among women the mortality is somewhat increased on account of their liability to suffer from metrorrhagia, or, when pregnant, from miscarriage or premature delivery. The occurrence of either of these accidents or the presence of the parturient state strongly predisposes the patient to the hemorrhagic form of the disease. The mortality

in men is, on the other hand, considerably increased by intemperance. Drunkards or constant imbibers seem particularly prone to suffer from hemorrhagic smallpox. We have found almost all forms of the disease more severe among bartenders. The powers of resistance against the exhausting influence of variola are often so diminished by chronic alcoholism that death results from a form of the disease from which a patient with more healthy organs would recover.

Mania a potu constitutes, of course, a very serious complication. Intemperate persons are apt to be badly nourished, and this condition is always unfavorable in smallpox.

It will be seen from the subjoined table that the mortality rate among males and females in our experience has been almost the same:

CASES AND MORTALITY ACCORDING TO SEX.

	Cases.	Deaths.	Percentage.
Male	4593	1267	27.45
Female	2606	670	25.71
Total	7204	1937	26.89

Unmodified smallpox is an exceedingly fatal disease, the death rate varying in different epidemics from 15 to 60 per cent. The epidemic which swept over this and other countries in the years 1870 to 1872 was everywhere characterized by unusual malignancy, and the mortality among the unvaccinated cases was, in some places, as high as 64 per cent. The following table shows the mortality rate among vaccinated and unvaccinated cases treated in the Municipal Hospital during the three largest epidemics experienced since its foundation:

MORTALITY RATE OF VACCINATED AND UNVACCINATED CASES IN DIFFERENT EPIDEMICS.

	Cases.	Deaths.	Percentage.
1871-1872. Unvaccinated	697	449	64.41
Vaccinated	1629	276	16.94
Total	2326	725	30.74
1881-1885. Unvaccinated	447	252	56.37
Vaccinated	551	81	14.70
Total	998	333	33.36
1901-1904. Unvaccinated	1943	636	32.73
Vaccinated	1844	124	6.72
Total	3787	760	20.06

It will thus be seen that different epidemics vary very greatly in malignancy. In 1901-04 the mortality rate among the unvaccinated was just one-half that observed in 1871-72, and almost one-half less than the death rate in 1881.

Indeed, smallpox may occur in epidemics in which the death rate reaches as low a figure, even among unvaccinated cases, as 2 per cent. Such a remarkable epidemic has been prevailing in various sections of the United States during the past few years.

In the absence of an epidemic influence, smallpox is usually much

less fatal. It is believed by some authors that the disease is more fatal at the beginning and during the maximum of an epidemic than when it is declining, but we are not sure that such is always the case. Certain seasons of the year are also believed to exercise some influence over the mortality from the disease. It is probably true that a patient is less able to bear the depressing effects of confluent variola when the weather is excessively hot than when the temperature is cooler.

Type of Disease.—In considering the prognosis in individual cases various circumstances are to be taken into account. The *type of the disease* and the *extent and depth of the eruption* are among the most important factors. The hemorrhagic form of smallpox is frightfully fatal. Indeed, it may be laid down as a rule almost without exception that recovery never takes place from the graver types of this disease. Of 152 cases of hemorrhagic smallpox observed during the epidemic of 1871-72, 146 died. The 6 cases that recovered belonged to the milder variety of this type; 1 had slight bloody vomit, and the other 5 exhibited an eruption which on some parts of the body was purplish, while a number of vesicles contained a dark-blue spot in the centre, showing that blood was exuded into the vesicles.

The next most fatal form of smallpox is the confluent variety. When it is comprehended that in such cases there may be forty thousand or more pustules present, the reason for the high death rate is apparent. Of 211 cases of confluent smallpox accurately observed during the epidemic of 1871-72, 168 died, showing a mortality rate of 79.62 per cent.

Semiconfluent cases are correspondingly less fatal than the confluent; while in cases with discrete eruptions the mortality falls to a comparatively low level.

Thus it will be seen that the prognosis in any particular case is influenced to an enormous extent by the character of the eruption. In varioloid or smallpox so modified by vaccination, inoculation, or previous attack that the secondary fever is slight or absent, the mortality is almost *nil*, as will be seen from the appended table:

VARIOLA AND VARIOLOID TREATED IN THE PHILADELPHIA MUNICIPAL HOSPITAL.

	Cases.	Deaths.	Percentage.
Variola	4156	1905	45.98
Varioloid	3048	31	1.01
Total	7204	1937	26.89

The fatalities in varioloid result, as a rule, from some complicating condition. It must be remembered that attacks in adult patients who were vaccinated in infancy and showed no appreciable protection are classed under the head of variola.

The stage of the disease at which death occurs in smallpox will depend somewhat upon the character of the attack. Patients suffering from hemorrhagic variola usually succumb on the fourth, fifth or sixth day of the eruption. Considering all types of the disease the largest

number of fatalities occur during the second week of the eruption and particularly upon the ninth, tenth, and eleventh days. As will be seen in the accompanying table, of 1019 fatal cases of smallpox, 575, or 56.42 per cent., died during the second week, and 347, or 34.05 per cent., of these expired on the ninth, tenth, and eleventh days. Basing the assertion upon these figures, it may be stated that over one-third of the fatalities occur upon the critical days mentioned, and over one-half of the deaths during the second week.

We have occasionally observed death to take place as late as five or six weeks after the onset of the disease, but in these cases the unfavorable termination has been brought about by some complicating affection.

**SHOWING THE PERIOD OF THE DISEASE AT WHICH 1019 CASES OF SMALLPOX
PROVED FATAL.**

First week :										
1st day of eruption	1
2d " "	4
3d " "	14
4th " "	81
5th " "	63
6th " "	90
7th " "	90
										— 293
Second week :										
8th day of eruption	84
9th " "	122
10th " "	114
11th " "	101
12th " "	75
13th " "	49
14th " "	30
										— 575
Third week :										
15th day of eruption	28
16th " "	22
17th " "	12
18th " "	9
19th " "	5
20th " "	8
21st " "	7
										— 91
Fourth week and after :										
22d day of eruption	7
23d " "	8
24th " "	6
25th " "	3
26th " "	4
27th " "	3
28th " "	5
29th " "	4
30th " "	4
31st " "	2
32d " "	4
33d " "	1
34th " "	2
35th " "	1
36th " "	3
37th " "	1
39th " "	1
44th " "	1
										— 60
Total										1019

Vaccinal Condition.—The vaccinal condition of the individual is a most potent factor in influencing the course of the variolous disease. The degree of protection conferred by the vaccine process can be, in most cases, approximately estimated by the character of the vaccine cicatrix. Every now and then we encounter patients with good vaccination scars from an infantile vaccination, in whom the protection against smallpox has been almost completely lost; and, on the other hand, we may see patients with poor scars who still enjoy considerable protection; but these may be looked upon as exceptions to the general rule.

The existence, therefore, of good cicatrices in a patient who is attacked with smallpox may be regarded as of favorable prognostic import.

Of 8893 cases of smallpox treated at the Municipal Hospital, 2335 presented good scars; of this number, 152 died, constituting a mortality rate of 6.5 per cent.; 1105 patients with fair scars were treated, of whom 135 died, showing a death rate of 12.21 per cent.; 1524 cases were admitted with poor scars, of whom 345 died, giving a death rate of 22.64 per cent.; 3687 unvaccinated cases were admitted, of whom 1542 died, giving a mortality rate of 41.82 per cent. Thus it is seen that the danger of attacks of smallpox can be measured with a considerable degree of accuracy by the vaccinal condition of the patient.

VACCINAL CONDITION AND MORTALITY RATE.

	Admitted.	Died.	Percentage.
Vaccinated In infancy (good scars)	2335	152	6.5
" " " (fair ")	1105	135	12.21
" " " (poor ")	1524	345	22.64
Postvaccinal cases	4964	632	12.53
Unvaccinated "	3687	1542	41.82
Unclassified "	242	45	18.18
Total	8892	2219	24.96

There is no reliable symptom during the initial stage to indicate the gravity of the attack. Not infrequently the mildest eruption of varioloid is preceded by a very severe febrile stage. If, however, the initial stage be very mild, it is safe to prognosticate a moderate eruption. Severe lumbar pains may be present both in modified and unmodified smallpox, yet if they be extremely severe there would be some reason to anticipate a hemorrhagic form of the disease. Inasmuch as the initial morbilliform exanthem (*roseola variolosa*) is most often seen in varioloid, we would regard the presence of this rash as an indication that the true eruption will be of modified form. When the rash is of the scarlatiniform type, the ensuing eruption may be moderate or severe; when, however, the prodromal rash is purpuric, it is a symptom of evil portent, preceding as it does the hemorrhagic form of the disease. There are, however, exceptions to this last statement; we have occasionally seen erythematopurpuric prodromal rashes in persons who have made perfectly good recoveries.

It has been already stated that the quantity and character of the eruption are accurate guides as to the gravity of the disease. The

condition of the mucous membrane of the pharynx, larynx, and trachea should be regarded as only second in importance to the skin lesions in estimating the degree of danger in variola. If these parts become severely implicated by the variolous process, giving rise to a diphtheritic condition of the fauces, dysphagia, difficulty of respiration, or œdema of the glottis, the case should be viewed with grave apprehension. Even hoarseness at the early period of the maturative stage should be looked upon with suspicion.

Favorable Symptoms.—As has been stated, mild initial manifestations and the occurrence of a roseolous rash are favorable, inasmuch as they precede, as a rule, mild forms of the disease. Even in profuse eruptions, if the pustules become prominent and acuminate well, and are accompanied by considerable swelling, and if those on the extremities are surrounded by a pinkish areola, and the patient takes nourishment freely, there is good ground for hope. At a more advanced period of the disease, if the state of the nervous system be tranquil and the patient passes quiet nights, has a contented disposition, and entertains a confident hope of recovery, the probability of a favorable termination of the disease is greatly increased, even though the eruption be severely confluent.

Unfavorable Symptoms.—Among the symptoms which indicate the approach of a hemorrhagic attack are: excruciating backache during the initial stage, a petechial prodromal rash in the axilla and groins, subconjunctival ecchymoses and hemorrhages from the various mucous membranes, a claret-colored areola about the lesions upon the extremities, and a bluish or lead-colored discoloration of the centres of the vesicles. The prognosis in a case presenting such symptoms would be almost hopeless.

An excessive degree of confluence on all parts of the body renders the prognosis extremely grave. It is an unfavorable sign in confluent cases if the pustules on the face be flat, milky-white in color, and pasty, and if there be absence of swelling. It is also ominous to see here and there on the face vesicles desiccating prematurely and producing flat, brownish scabs.

During the early period of inaturation the patient's condition should be regarded as extremely critical if the progress of the eruption be suddenly arrested and the swelling of the face and hands subside, leaving the skin between the pustules pale; if the pustules themselves shrink and collapse; if the pulse be rapid, dicrotic, or feeble; if the delirium and restlessness increase; or if nourishment be refused or taken very reluctantly.

Valuable information may often be gained by observing the nervous symptoms, especially at an advanced period of the disease. Great restlessness, insomnia, despondency, constant moaning and grinding of teeth in children, are unfavorable symptoms. Violent and protracted delirium, convulsions, or coma usually preclude all hope of recovery.

Even after the patient has passed safely through the perils of the regular stages of variola, his life may again be placed in jeopardy by

certain complications. Fortunately, those which are most frequent—furuncles and abscesses—rarely lead to a fatal issue. The occurrence of pneumonia, pleuritis with effusion, erysipelas, or abortion should be viewed with deep concern. But the most fatal of the complications liable to arise are suppuration within the joints, pyæmia, and empyema. Gangrene of the scrotum and glossitis variolosa arising earlier in the course of the disease usually portend a fatal outcome.

THE TREATMENT OF SMALLPOX.

The treatment of smallpox may be considered in its relationship, first, to the patient himself, and, second, to the community at large. The latter aspect of the subject concerns the prophylaxis or preventive treatment of the disease. This may be conveniently classified under the following captions—notification, isolation, surveillance or quarantine, disinfection, and vaccination.

Prophylaxis. Notification.—It is important in the interests of public health that the existence of a case of smallpox should be promptly made known to the proper health authorities. It is usually the duty of the physician in attendance to transmit this intelligence. Every practitioner of medicine should feel himself called upon to aid and sustain the sanitary authorities in their efforts to prevent or stamp out a pestilential disease and should willingly comply with any arrangements whose object is the attainment of so desirable an end.

Most large communities have enacted laws making compulsory the notification of smallpox and other pestilential diseases, under pain of fine or imprisonment. It is only through a knowledge of the distribution and extent of smallpox in an infected district that the health authorities are enabled to intelligently and efficiently inaugurate measures toward its suppression.

Isolation.—It is of paramount importance, when smallpox appears in a community, to prevent the dissemination of infection; to this end the isolation of the patient—the source of the infection—becomes essential. This can only be accomplished with any degree of certainty by having the sick removed to a well-organized hospital. General hospitals and other public institutions cannot, with justice to the other patients or inmates, harbor and treat those suffering from smallpox. Even the caring for such patients in isolated pavilions in general hospitals is open to the objection of multiplying the foci of contagion in the city or town. It follows, therefore, that every city and large town should be provided, either temporarily or permanently, with a special institution for the treatment of this disease in the event of its outbreak. It should be located in a healthful district, sufficiently removed from the thickly settled portions of the city to preclude the possibility of transmitting the contagion to inhabited domiciles, but not so remote as to interfere with its accessibility. It is also of importance that such institutions should be constructed in a modern manner, with a view to making the unfortunate patients as comfortable as possible.

Of course, a special hospital of this character should be managed under strict quarantine regulations. No person, however well protected, should be allowed to visit a patient in the institution except under extreme circumstances, and then only after every possible precaution shall have been taken to prevent his carrying away the infection. The nurses and attendants should not be allowed to leave the hospital, nor come in contact with other persons, until they have had an antiseptic bath and have changed their infected clothing. In providing nurses and other employés for the hospital it need not be required that they shall have had smallpox, but they should invariably be vaccinated or revaccinated before entering upon duty. When delay is possible it is wise to await the result of such vaccination before the individual is brought into the infected atmosphere. The hospital should be supplied with closed ambulances for the transportation of patients. Private or public vehicles should never be used for this purpose. Indeed, this is regarded as so important a matter that in some large cities in this country the use of any kind of public conveyance for carrying persons afflicted with smallpox is prohibited by law, and its infringement is made punishable by fine.

Lest infection be spread by the ambulance itself it should be disinfected and provided with clean bedding, blankets, etc., every time it is used. In order that the public may know the character of the disease that it conveys, it should bear the name of the hospital to which it belongs.

If the smallpox patient is to be treated at home, every possible effort should be made to seclude him from all persons, excepting only such as are required to act as nurses, and they should be protected by recent vaccination. In selecting the apartment for the patient, a room most completely separated from all other parts of the house is to be preferred. If this is not practicable—which is usually the case in the ordinary city residence—the uppermost room of the house should be preferred. It should be well ventilated, and, if possible, have an open fireplace in which fire should be kept constantly burning. All unnecessary articles of furniture, such as drapery, upholstery, carpets, etc., should be removed. Every precaution in regard to cleanliness and disinfection of bedding, clothing, and everything in use in the room should be exercised, so that the danger of spreading the infection shall be reduced to the minimum. A sheet wrung out in a strong solution of carbolic acid, Labarraque's liquid, or some other disinfectant, and suspended across the doorway may aid in preventing the infection from being disseminated to other parts of the house. The spaces around doors that are not in use, which communicate with parts of the house to be protected, should be sealed by pasting strips of wrapping paper over them.

Surveillance or Quarantine.—When smallpox appears in a house, the question arises, What shall be done with the exposed but well members of the household? If the patient is treated at home, the other inmates as well as the sufferer should be quarantined. For, if removed to another locality, save to a quarantine station or hospital, the disease

might subsequently appear there, and a new centre of infection be thus established. To depend upon people voluntarily to curtail their personal liberty for the public good would be confiding too much, at the present time, in human benevolence and public spirit. Therefore, the best results will be obtained, when the patient is retained at home, by stationing reliable guards about the house to enforce detention of the exposed inmates and also all other necessary precautionary measures.

On the other hand, when the patient is removed to the hospital it is, in our judgment, not necessary to enforce the above-mentioned restrictions. Indeed, we are of the belief that the object desired is often defeated in large cities by a routine quarantine of the inmates of houses from which smallpox patients have been removed. To make such a quarantine effective the individuals should be detained for a period of eighteen days, the outside limits of the stage of incubation. Segregation of the inmates of the household for so long a period works a great personal hardship and prompts them, in many instances, to escape before the quarantine is placed upon the house. We have known persons frequently to flee from houses where there existed an individual suspected of having smallpox, but in whom the diagnosis had not been definitely made. The settling of these exposed persons in different parts of the same city and in other cities results in the outbreak of the disease in these various localities. Thus, instead of limiting the infection rigid quarantine laws may favor its dissemination. Furthermore, unpopular restrictive measures tend to provoke evasion of the law and concealment of the existence of the disease.

When the patient is removed to the hospital we would advise immediate vaccination of the exposed individuals. To avoid, as far as possible, failures through imperfect virus or technique, three or four insertions with different virus had better be made. At the same time there should be thorough disinfection of the infected articles and apartments. After this has been accomplished the exposed individuals might resume their freedom. They should, however, be kept under medical surveillance, and should be daily visited by a physician who should watch for any symptoms of variola. Such inspection should be continued for sixteen days from the onset of the disease in the original patient, at the end of which time the suspected individuals, if well, may be exempted from further surveillance. During his visits the physician can determine whether the vaccinations are "taking," and, if not, the procedure can be repeated, thus giving the patient a still further chance of protection if vaccinal susceptibility exists.

The above plan is based upon the assumption that smallpox is not contagious during the period of incubation, and this view is in accord with the belief held by practically all authorities on the subject. Until active symptoms manifest themselves the exposed individual is not a menace to the health of the community, and it is unnecessary and injudicious to restrict his liberty during this period. Furthermore, a large experience has demonstrated to us that under a system such as

outlined, a *much larger percentage of exposed individuals will submit to vaccination and a correspondingly increased number of patients will consent to be removed to the hospital*, for only those who comply with this advice will be exempted from quarantine.

Apart from these considerations, the system of routine quarantine, during epidemic prevalence of smallpox, will be found to involve the expenditure of large sums of money.

The quarantining of exposed persons may be practicable and wise in dealing with sporadic cases of smallpox or with the first cases in a community, for under such circumstances extraordinary precautions are justified in an endeavor to limit the outbreak of the disease to the original patients.

Another means of restricting the spread of smallpox is to apprise the public of the particular locality in which the disease exists, so that no one may unknowingly approach within infecting distance of the place. But how to do this without exciting unnecessary alarm is a problem not easy of solution. The plan adopted in some cities of *placarding* the infected house with a large and conspicuous poster is believed by many to serve a useful purpose, notwithstanding the fact that it frequently meets with much opposition. But whether this plan be adopted or not, the sanitary authorities should keep the premises under constant supervision, instituting daily visits by officers qualified and empowered to advise and direct the observance of proper sanitary precautions.

Disinfection.—Disinfection is a highly important prophylactic measure. The infection of smallpox is not only imparted to the atmosphere surrounding the patient, but to all articles which have been used by him or have been near him. It clings to these articles for a variable length of time, and they are, therefore, not infrequently the media by which the infection is conveyed to others. Disinfection consists in the complete destruction of the infecting agent of the disease. Fresh air and sunlight are nature's disinfectants; when infected articles are freely exposed to the atmosphere and rays of the sun for some time the infecting principle becomes less and less active, and finally disappears. Therefore, the house, especially the room, occupied by the patient should be freely though cautiously ventilated. If the weather be cool, an open fire upon the hearth would consume much of the infected atmosphere.

Chemical substances, however, furnish the more speedy and reliable disinfectants, and it is upon such that we mainly depend for the destruction of the disease germs. Some agent of this nature should be brought directly in contact with all the excrementitious matter from the patient, and with everything that has been used by him or has been near him during the progress of the disease. All discharges, not excepting those from the mouth and nose, should be received into a vessel containing some such disinfectant as chloride of lime, carbolic acid, or bichloride of mercury. Under no circumstances should the excreta be allowed to flow into the sewer or be cast away without first having undergone

disinfection. In country districts, where disinfectants may not be readily obtained, the discharges should be deeply buried in the ground in a locality where there is no danger of contaminating the water supply. Every handkerchief, towel, and article of bedding and clothing used by the patient should be steeped for some time before leaving the room in a solution of two fluidounces of chloride of zinc or four fluidounces of carbolic acid to the gallon of water, and afterward boiled by themselves for half an hour or longer in plain water; all small articles, such as bits of linen, sponge, absorbent cotton, and the like should be burned immediately; all utensils used for eating and drinking should be purified by boiling water; and, in short, nothing should be allowed to leave the room without having first been subjected to some form of disinfection.

The attendants should not be more numerous than the necessities of the case require. They should be carefully instructed in regard to the importance of cleanliness, disinfection, and isolation. Not only should they be instructed to exclude from the sick-room all persons not having authority to enter, but also all domestic animals, such as the dog and cat, as they are exceedingly liable to serve as conveyers of the infection.

The clothing of the attendants should be of such material as can be readily boiled and washed, and it should be frequently changed and subjected to this process. No attendant while engaged with the case should come in contact with other persons. On leaving, either temporarily or permanently, a bath should first be taken, using freely carbolic acid soap, and the hair should be washed with a solution of mercuric chloride. No clothing that has at any time been in the infected atmosphere should be worn or carried away from the premises, unless it has first been disinfected.

Physicians should also exercise care lest they may be the means of communicating the infection. When called upon to attend a case of smallpox the physician should not remain in the infected atmosphere longer than is necessary to make a proper examination; the prescription may be written and advice given in another apartment. After each visit he should carefully wash his hands, face, and hair; his hands especially should be washed in some disinfecting solution. He should then expose himself for a considerable time in the open air before visiting another patient.

The physician should wear in the sick-chamber a long mackintosh or a linen duster buttoned up to the chin, and a cap to cover the hair, and these garments should be kept hanging in the open air in the intervals of his visits. In hospitals where there are many patients to be examined, and where he is required to spend considerable time in the wards, nothing short of a change of his entire outer clothing before leaving the institution should be considered. It is also of importance for the physician to cover his shoes with rubbers, so that no variolous crusts which may be upon the floor will be carried out of the infected house.

The isolation of a smallpox patient should be continued until all the scabs are removed. The time necessary to effect their separation varies greatly in different cases. In severe confluent forms of the disease a month or more will be required, while in extremely mild and abortive cases of varioloid the skin may be entirely smooth in a week or ten days. Upon the palms and soles the inspissated pocks remain embedded for a long time and require mechanical removal in order to avoid a long and tedious waiting for spontaneous exfoliation. Even after removal of the variolous crusts the patient should not be allowed to associate with the public until he has had one or more antiseptic baths. Perhaps the most reliable antiseptic bath that can be given is one containing corrosive sublimate. The safest way one may proceed in the use of such a bath is by simply sponging the body and carefully wetting the hair with the solution (1:2000) and then have the patient freely bathed in plain water with the use of carbolic acid soap, or the patient may take a full bath in a tub containing a 1:10,000 or 1:20,000 solution of mercuric chloride. A 5 per cent. solution of Labarraque's liquid also makes a very reliable disinfecting bath. After this he should put on clothing which has not been exposed to the infection, or, if exposed, has been disinfected, and he may then safely mingle with the public.

Inasmuch as the body of a person who has died of smallpox is capable of imparting the infection, some precautions should be observed in regard to it. For instance, the body should be thoroughly wet with a solution of corrosive sublimate (1:1000) or with a solution of chloride of lime in proportion of six ounces of the drug to a gallon of water, or with some other equally powerful disinfectant; besides, it should be wrapped in a sheet saturated with one of these solutions and buried at once. The preferable method of disposing of the dead from this disease is by cremation; but this method is yet perhaps too strongly opposed by public sentiment to be practicable. It is not advisable to transport the corpse a long distance or from one city to another for burial, but if this be really necessary, it should first be placed in a metallic coffin hermetically sealed. In its burial it should be put at least six feet under ground, and should not be disinterred unless absolutely necessary, and then only under sanitary supervision. The vehicle used for conveying the body to the grave should afterward be disinfected. It is, perhaps, unnecessary to say that the funeral should by no means be public.

After the sick chamber has been vacated, either by recovery or death of the patient, every article it contains of no great value should be immediately burned. Everything else which will not be injured by the ordinary operation of the laundry may be safely and cheaply disinfected by immersion in boiling water for half an hour. It should be remembered, however, that the water must be maintained at the boiling point for that length of time. But if it is impracticable to subject such articles at once to the boiling process, they should be immersed for about four hours in some reliable disinfecting solution—such as $\frac{1}{2}$ mercuric chloride

in the proportion of 1:2000, or carbolic acid 1:50--and subsequently boiled.

The sick-room should be disinfected according to the principles laid down in the chapter on disinfection. The room should then remain closed from twelve to twenty-four hours, afterward opened, thoroughly ventilated, and all surfaces, including the furniture, washed with a disinfecting solution (chloride of lime, carbolic acid 1:50, or mercuric chloride 1:1000); afterward the floor and other woodwork should be thoroughly scrubbed with soap and water. The wall-paper, if there be any, should be well moistened with the carbolic acid solution and scraped off and burned. Paper may be reapplied or the walls white-washed, according to fancy. In addition to all these precautions, it is advisable to have the room remain unoccupied for three or four weeks, during which time it should be well aired.

For disinfection of outer clothing, carpets, bedding, and all articles which cannot be boiled, there is nothing superior to steam under pressure. The germs of smallpox will certainly perish if exposed for half an hour to this agent at a temperature of 230° F. There are, however, certain articles which would be injured by moist heat, and for the disinfection of these dry heat may be substituted. In this case a temperature of at least 230° F., continued for two hours, will be required. Formaldehyde, however, could be used instead of dry heat.

Vaccination.—Of all of the measures employed to prevent the spread of smallpox, none is so important and efficacious as Jenner's great discovery. There is perhaps no single scientific fact better established than that vaccination, periodically repeated, is capable of effectually preventing the occurrence of that disease in man. In view of this fact it does at first sight seem strange that variola should continue to prevail in civilized communities; and, while nothing appears easier than to control the spread of this disease, or even to eradicate it altogether, yet there are difficulties in the way of accomplishing this end which seem almost insurmountable. These arise from various causes, but chiefly from individual carelessness or indifference about employing vaccination, and from the absence of a general law making it compulsory. We know that many conscientious citizens are opposed to enforcing vaccination by law, but as every unvaccinated person is liable to contract smallpox and disseminate the infection among others, he should be regarded in the light of a public enemy, and dealt with accordingly. Surely it is not an unreasonable position to assume that no person through ignorance or prejudice should be allowed to contravene the public welfare.

But, in the absence of a statutory law requiring the vaccination of all persons, very much can be done in the way of enforcing the measure by restricting the privileges of the unvaccinated. For instance, satisfactory evidence of successful vaccination should be required of every child before admission into public and private schools and institutions for the care of children; no unvaccinated person should be allowed to serve as a soldier in the army or navy, or in the State militia; and no

unvaccinated immigrant should be allowed to land until vaccination has been performed.

In view, therefore, of the great importance of this prophylactic measure, it becomes the duty of all municipal and State authorities to provide gratuitous vaccination for the poor, and, indeed, for all helpless children of careless or improvident parents, no matter to what class of society they belong. No expenditure of money should be spared by these authorities in order to protect their citizens against a disease so loathsome and fatal as smallpox. From a purely monetary point of view such expenditure is wise, for a single epidemic of this much dreaded disease in a community may necessitate a greater outlay to care for the indigent sick alone than would be required to purchase the means of protection for that community for a decade of years.

If vaccination were universally practised, and repeated from time to time as circumstances required, there would be little need for other means of prevention. Whenever a case of smallpox occurs in a family, the physician's first duty is to vaccinate promptly all members of the family who have never been vaccinated, and revaccinate all others without regard to the character of their previous vaccination. It is a good plan to vaccinate on several successive days those who have never been previously subjected to this procedure, in order to increase the probability of obtaining a successful result. If this be done and the patient sent to the hospital, the disease may be prevented from spreading.

Care of Patient.—In order to consider in detail the treatment of smallpox it seems most convenient to divide the disease into its various stages, as follows: (1) the stage of incubation; (2) the initial stage; (3) the eruptive stage; (4) the stage of suppuration; (5) the stage of retrogression, or stadium exsiccationis.

1. The Stage of Incubation.—The interval between the reception of the infecting agent of smallpox into the blood and the earlier manifestations of the disease is usually unattended by symptoms. There is no doubt, however, that certain unknown processes take place during this period. It is very important to know whether anything can be done at this time to arrest or change these processes so as to prevent or modify the approaching disease. Drugs, of course, are powerless for this purpose. Is vaccination at this period capable of exerting any such influence?

From the clinical reports of those who have made extensive use of vaccination at this period of smallpox there seems to be some differences of experience concerning its efficacy. In commenting on this question Curschmann says: "Are we able to exert any influence on the disease in the early stage preceding the eruption? Is it possible in infected persons, during the stages of incubation and invasion, to cut short the disease or to modify its course? Many attempts have been made to answer these questions affirmatively, but as yet without much result. The first idea was vaccination, and this was employed by some in the ordinary way; by others subcutaneous injections of vaccine lymph have been given, it is said with good results. I must, however, advise great

skepticism regarding these assertions. Of the subcutaneous injection of lymph I have no experience; but that ordinary vaccination during the stages of invasion and incubation cannot stay the disease has been proved to me by chance observations and direct experiments. On the contrary, I have seen, in cases in which vaccination was practised after infection with variola, vaccine pustules and smallpox pustules developed side by side. It is, in my opinion, very doubtful whether vaccination can even render the course of the disease milder."

The hypodermic use of vaccine lymph is certainly not entitled to any confidence as a prophylactic measure. Immunity does not result from the mere presence of vaccine virus in the blood, but from certain unknown processes which take place in the system in the course of true vaccinia.

It is, therefore, evident that the vaccine disease must reach a certain stage of development before it is capable of exerting any prophylactic power whatever. We have had very frequent opportunities of observing that vaccination during the invasive or initial stage of smallpox is utterly valueless, and also that it is equally useless when performed only three or four days prior to the earlier invasive symptoms. A vaccine vesicle resulting from a vaccination performed at the period just mentioned, and the variolous pustules, will, it is true, develop side by side without the one exerting any influence whatever over the other. But, Curschmann's experience seems to warrant the inference that at no time within the incubation period of smallpox can vaccination be used with advantage against the approaching disease. If such is his experience, it certainly differs very greatly from our own. We have in numerous instances seen smallpox very markedly modified by vaccination performed at this period, and not infrequently have seen it prevented absolutely. In order that protection shall be complete it is necessary that the insertion of the vaccine lymph should be made almost immediately after the reception of the contagium; but if made at a somewhat later date a modifying effect may still be obtained. No part of the incubation period should be considered too late to make use of this remedy, since this period is sometimes prolonged beyond its usual limits, in which case a late vaccination may prove of value.

It is our opinion that vaccinia does not begin to exert its prophylactic power until the areola commences to form around the vesicle. At this time the mild febrile reaction, which was regarded by Jenner as a *sine qua non* in true vaccinia, becomes apparent. If this stage of the vesicle be reached before the patient shows any symptoms of smallpox, the disease may be entirely prevented; if not reached until after the febrile symptoms appear, but before the eruption occurs, it may modify the attack. Now, it is well known that in typical vaccinia the areola appears about the seventh day or eighth day from the date of insertion of the lymph, and is at its height on the ninth or tenth day; and it is equally well known that the incubation period of variola is, in the majority of cases, of ten or eleven days' duration, and that the eruption does not appear until about three days later. This renders quite obvious the fact that vaccination, practised shortly after variolous infection has

occurred, has an opportunity in point of time to exert more or less prophylactic influence against the incubating disease. While no inflexible rule can be laid down, it may be said in a general way that if vaccination be practised on the first or second day after the reception of the infection into the system, the protection may be perfect; and if employed between this date and the fifth day, it may be partial. But we would emphasize the fact that after infection has occurred, every day that is allowed to pass before resorting to vaccination is so much valuable time lost.

While the appearance of the areola generally indicates the period of the vaccine process at which its prophylactic power begins to be exerted, yet this period may vary somewhat in different individuals. For instance, we have more than once seen, say, two persons exposed to the contagion of smallpox at the same time in such a manner that there could be no doubt about infection having occurred, have vaccinated these persons at once and with the same virus, and the vaccinia in both cases has pursued an identical course, yet in one the protection was perfect, while in the other it was only partial. In other similar instances one has received partial protection and the other none at all. This difference is doubtless due to some individual peculiarity that cannot be explained.

It is much easier to confer protection against smallpox after infection, where revaccination is required to accomplish this result, than where the vaccination is primary. The explanation of this is not difficult. It is because vaccinia in its modified form, such as results from revaccination, develops more speedily, arrives at the areolar stage more quickly, and runs its entire course several days sooner than does the unmodified or true vaccinia; hence, it is clear that the period of protection in such cases must be reached earlier.

In endeavoring to confer protection during the incubation stage of smallpox the quality of the vaccine lymph employed has a great deal to do with the success. Nothing is of more vital importance at this period of the disease than that the vaccine virus employed should be fresh and active. The difference between success and failure in producing vaccinia after exposure often means to the patient the difference between life and death. We know of no virus more reliable or which will give better results than eighth-day lymph taken directly from a typical vaccine vesicle on the arm of an infant.

While humanized¹ virus has gone out of use in most countries, we cannot refrain from testifying to its reliability and value in persons who are exposed to smallpox. The virus of long humanization possessed the additional advantage of running a rapid course and so bringing about its protective influence promptly.

The virus resulting from a long series of human transmissions was, therefore, to be preferred over virus of recent humanization and animal virus. At the present time, however, we are more concerned with bovine virus, which has for certain reasons largely superseded the use of humanized lymph.

¹ Humanized virus is still extensively employed in Mexico, where the physicians prefer it to animal lymph.

It is believed by some authors that multiple insertions quicken the process of vaccinia, and thus hasten the attainment of that stage of the disease at which its prophylactic power begins to be exerted. Waterhouse was of this opinion, and his remarks on the subject are interesting because they were made a century ago, in the very earliest history of vaccination. He wrote:

"I think it proper to publish an important fact for which we are not indebted to Europe, namely, *If a person be inoculated with the kinpock two days after having received the casual infection of smallpox, the kinpock will predominate and save the patient.* Nay, I will go further and say in some cases *three days* posterior to infection instead of two; for there is a mode of expediting the operation of the kinpock virus by increasing the quantity of matter thrust under the epidermis; and it appears, from experiment, that this does not depend so much on increasing the quantity put into a deep puncture as it does on the increase of infected surface. In other words, you may expedite the process of kinpock inoculation two days if not three, if, instead of two punctures, you make sixteen or twenty; . . . and on the sixth day from the operation we shall have the appearance of the eighth day in ordinary cases; and on the eighth day we shall find the appearance of the tenth, and so on with the febrile symptoms, in which commotion the prophylactic power consists."

As there is nothing at this stage of smallpox of greater importance than vaccinia attended by prompt and speedy development of the vesicle, it is evident that the virus employed should be selected and used with the greatest possible care and skill.

It is well under these circumstances to employ an active virus; the production of a sore arm is a matter of but little importance when the exposed individual's life is at stake.

In order to ensure success, *it is advisable to employ virus, when possible, from more than one source.* It is desirable at this time to guard as far as possible not only against failure, but also against a vaccine disease of slow progress. A tardy vesicle, or one that is slow in making its appearance and late in arriving at maturity, gives no assurance of safety.

In recent years animal lymph has been brought to a high state of perfection by the admixture of glycerin. We have found glycerinated lymph properly prepared and preserved to be more likely to succeed and also more speedy in its action than the dried virus on ivory points. Hence, during the incubation period of smallpox glycerinated lymph may be found almost, if not quite, as effectual as long humanized virus in preventing or modifying the approaching attack. We have had extensive opportunities of testing its power in this direction and have been well pleased with the results. The records of the hospital bear testimony to the fact that during the recent epidemic of smallpox in Philadelphia several unvaccinated persons sent in through error of diagnosis were protected absolutely by the use of glycerinated lymph. Where the protection was not perfect there was marked modification

FIG. 51



showing the coexistence of smallpox and vaccinia, the vaccination having been performed six days before the appearance of the varicelous eruption. Little or no modification.

FIG. 52



Smallpox and vaccinia running a coincident course, the vaccination having been performed about three days before the appearance of the varicelous eruption. Photographed on eighth day of eruption.

SMALLPOX

se. Of course, vaccination was performed as soon as possible
tion.

--- The fullest effort to ensure success it is advisable to vaccinate
--- person each day for two or three days in succession. It
that the individual should have an excessively sore arm
in an unmodified attack of smallpox.
served the effects of vaccination during the period of
370 cases. The vaccinations were all primary and were
various periods of this stage—from immediately after
of the infection until two days before the appearance of

report of the statement already made, namely, that the vaccine
is not be so exert its pro ylaetic power until the vesicle
i the s at which the eola appears, we present the
table:

PATIENTS VACCINATED AFTER EXPOSURE.

	Cases.	Deaths.	Percentages
Vaccinated seven days or less before the variolous eruption	106	39	36.79
Vaccinated more than seven days before the variolous eruption	264	38	14.77
Total	370	77	21.06

From these figures it is conclusively proven that, the earlier the vaccination is performed during the period of incubation, the greater is the chance of the disease being favorably modified.

Some of the deaths occurring in patients vaccinated more than seven days before the eruption may be attributed to a too tardy development of the vaccine lesion. Most of the patients were vaccinated with bovine lymph, and it is known that this lymph, particularly when used in the form of dry points, is slower in its effect than humanized virus or glycerinated lymph.

Forty-seven persons vaccinated for the first time by us after exposure to smallpox were perfectly protected against the disease. As these individuals were all under observation in the hospital, where they came in the closest possible contact with smallpox patients, there can be no question that the contagium was present in sufficient quantity to ensure immediate infection.

2. The Initial Stage.—The initial stage of smallpox comprises the period between the earliest manifestation of the disease and the appearance of the eruption, and has a duration usually of about three days. After what has been said of the inutility of vaccination after symptoms appear, or of the hypodermic use of vaccine lymph, recommended by Furley, it is needless to consider further either of these means as a remedy at this stage of the disease. Bloodletting, formerly so much employed, is now almost never resorted to, not even for the relief of symptoms. Quinine, in large doses, has been recommended as exerting a favorable influence over the course of the disease, but the experience of Curschmann and others show that it possesses no such value. In short, all attempts to stay the disease, or even modify its course, have

proved unavailing, and we can do nothing more at this stage than treat special symptoms as they arise.

The popular though erroneous notion of past centuries, that it is necessary to keep the patient hot and sweating, still prevails to some extent, and not infrequently it is found very difficult to overcome this prejudice. On the contrary, every effort should be directed toward keeping the patient as comfortable as possible, and experience shows that a bedroom well ventilated and having a temperature of from 65° to 70° F. is best suited for this purpose. The ordinary febrifuge mixtures, such as liquor ammoniæ acetatis, liquor potassi citratis, tinctura aconiti, etc., may be given in suitable doses and at stated intervals. We are in the habit of using the following formula:

R—Spirit. æther. nitrosi,
Syrup. limonis āā f3iv.
Liquor. ammonii acetatis f3v.—M.

Sig.—Give 2 to 4 fluidrachms every two hours in a little ice-water.

If there is irritability of the stomach, the effervescing citrate of potassium may be preferable. It sometimes happens that the stomach is very irritable, especially in children; in this case lime-water, subnitrate of bismuth, aromatic spirit of ammonia, a little chloroform-water, or any other drug or agent known to be of service in this condition, may be used. The swallowing of small pieces of ice will often give relief when everything else fails. When the skin is hot and dry and the temperature high, frequent sponging with cool water is serviceable. Severe headache may call for the application of cold water, iced compresses, or an ice-bag to the head. These need not be feared on account of the popular superstition that they tend to suppress the eruption, for such is not the case.

Nervous symptoms, such as insomnia, delirium, and convulsions, are often prominent features of the disease and demand appropriate treatment. Some of the bromide salts, or chloral, given either separately or in combination, will usually succeed in subduing these symptoms. For the convulsions of children there is perhaps nothing more effective than chloral, given either by the mouth or rectum. When given by the mouth it should be well diluted, since it is very irritating to the throat, which is liable to become implicated in the variolous process quite early. Warm baths are also very useful. There is another nervous symptom commonly present at this stage of smallpox, and that is pain in the back. This is sometimes so distressing as to call for measures of relief. When the stomach is retentive Dover's powder may be given, or some one of the analgesic coal-tar products, now so frequently used to relieve pain. Sometimes there is much restlessness and general irritability; in such cases we have found a little morphine, combined with the febrifuge prescription above referred to, to act most happily.

The common practice of applying mustard to the back for the relief of pain or to the epigastrium to lessen gastric irritability cannot be too strongly condemned, since the variolous eruption always appears in much greater abundance on irritated surfaces. Wherever there is an

ulcer, a wound, or an excoriated condition of the skin, there the pustules are sure to be found in dense clusters. We have frequently seen the eruption intensely confluent over regions of the skin where a mustard plaster had been applied during the initial stage of the disease. Some have thought that the eruption might in this way be diverted from the face to other localities, but we are convinced that it is not diminished anywhere else by reason of its confluence on these parts through the action of a sinapism; rather is it increased to that extent.

The digestion at this stage is not vigorous; hence the diet should be light and easily assimilable. There is nothing more suitable than animal broths and milk. The best beverages are cold water and iced lemonade. Acidulated drinks seem to be particularly grateful to the palate. Gentle cathartics may, of course, be administered whenever indicated.

3. The Eruptive Stage.—The eruptive stage may be said to comprise a period beginning with the first appearance of the eruption and ending when pustulation has fully occurred. The duration of this stage in variola vera is usually seven or eight days, but in modified smallpox it is shortened in proportion to the degree of modification. The great desideratum for this period of the disease is a remedy capable of diminishing or modifying the cutaneous manifestations, for there is no doubt that recovery of the patient almost always depends upon the quantity of the eruption and the length of time consumed in running its course.

Formerly it was thought that some modification might be brought about by bloodletting, but experience shows that the most confluent eruption has succeeded the most vigorous employment of the lancet. It is, therefore, worse than useless to bleed, for by so doing we expend power that will be required later on to repair the injury done by the disease.

The treatment during the eruptive stage of smallpox should be directed toward alleviation of the subjective symptoms and the correction of special symptoms as they arise. Usually it is not until the eruption appears that the disease is recognized and the degree of severity prognosticated. If the case promises to be at all severe, all flannel undergarments should be at once removed, and the hair cut close, so that the head may be kept cool, cleanliness enforced, the risk of cellular inflammation of the scalp diminished, and a better opportunity afforded for the employment of cold applications should delirium or more urgent brain symptoms arise.

The febrile symptoms which usher in the disease now usually remit, but increase again as the eruption progresses. For this condition the remedies already mentioned may be continued. It sometimes happens in a depressed condition of the system, particularly in children, that the extremities and even the surface of the body are cool, and that the eruption is too slow in making its appearance. In such cases the application of heat and the administration of hot stimulating drinks, such as hot toddy, may be of service. This condition in children is apt to be associated with convulsions, in which case there is nothing better than

a warm bath followed by an envelopment in warm blankets. Should the convulsions continue, however, chloral, by either mouth or rectum, is quite sure to give relief. We repeat here the caution not to fail to dilute the chloral freely, for the throat is now so much involved in the variolous process that an irritating draught may give rise to croupous symptoms, or even acute œdema of the glottis.

TREATMENT OF THE THROAT.—As the eruption progresses, not only the fauces, but the soft and hard palate, the buccal mucous membrane, the larynx, and sometimes the trachea also become more or less involved in the process, and this is often the source of difficult and painful deglutition. This condition requires the use of mouth washes and gargles, such, for example, as those containing chlorate of potash, boric acid, glycerole of tannin, tincture of myrrh, etc. We have found the milder demulcent fluids made from flaxseed, gum arabic, or slippery-elm bark particularly grateful. Of these none is more relished by the patient than flaxseed tea, sweetened with white sugar and acidulated with lemon-juice. Careful and frequent cleansing of the mouth affords considerable relief. This may be done by the nurse covering her index finger with a piece of soft linen, dipping it into a solution of boric acid with glycerin added, and then thoroughly and carefully cleansing the entire buccal cavity.

During the recent epidemic (1901–04) through which we have passed, we found orthoform, in one-grain lozenges, useful in lessening the distressing soreness of the throat and mouth. In severe cases, however, where the throat was covered with lesions we were obliged to use a cocaine (1 per cent.) spray in order to lessen the pain in swallowing, and thus enable patients to partake of sufficient nourishment. Variolous patients, according to E. Pepper, who advocates cocaine internally in smallpox, show a considerable degree of tolerance toward this drug. We have never noted untoward results from the employment of cocaine internally or in spray form.

The pain in the throat and difficulty in swallowing are often benefited by having the patient hold in his mouth small pieces of ice, and allowing these to dissolve slowly. Where there is much glandular swelling the application of the ice-bag externally will be found useful. Some patients, however, will prefer the use of poultices or hot fomentations. When there is much fœtor some antiseptic, such as carbolic acid or permanganate of potash, may be added to the mouth wash or gargle. We have found dilute chlorine water to answer a good purpose. Variolous glossitis is best treated by mild antiseptic mouth washes and the use of pellets of ice. Should acute œdema of the glottis or of the ary-epiglottic folds occur, an emetic may be given if the patient is not too weak, or local scarification may be practised. When suffocation threatens, tracheotomy offers the best if not the only chance of recovery.

TREATMENT OF NERVOUS SYMPTOMS.—Toward the latter part of the eruptive stage of variola persistent insomnia and delirium often occur. When this condition of the patient is attended by a flushed face and bounding pulse, an ice-bag to the head and a brisk cathartic may be

of service. Tartar emetic and sulphate of morphine, in doses of from one-eighth to one-half grain each, will often produce sleep and quiet the delirium. Morphine is a most valuable drug in controlling restlessness and inducing sleep during the pustular stage of smallpox. To accomplish this end, it is sometimes necessary to administer a half or three-quarters of a grain of the drug in twenty-four hours. However, it is usually well borne and the patients are almost always benefited by its use. Large doses of bromide of potassium, or chloral freely diluted, may be given, and repeated if necessary. Some care, however, must be taken not to push these remedies too far, lest the patient lapse into coma or a state of profound prostration.

Occasionally the delirium is of that violent kind which the older writers styled "delirium ferox." This is accompanied by a wild expression of the countenance, and such a strong tendency to escape from the attendant, or to self-destruction, that too much care cannot be exercised for the safety of both the nurse and the patient. We have known strong and muscular patients, while in this state of mind, to knock the nurse down, jump out of the window, and run to some secluded place, where they would cunningly secrete themselves. We have also known patients to attempt suicide in various ways while the nurse was temporarily absent. The necessities of the case, therefore, often require the use of some artificial means of restraint. For instance, a wide band of stout webbing or canvas may be placed loosely over the patient's chest and secured to each side of the bed. Smaller bands of the same material may be fastened to each wrist and ankle, or leather wristlets and anklets may be used, the former being secured to the sides of the bed, and the latter to the foot of the bed, allowing, however, a little motion of the limbs, so that the patient shall not be subjected to painful restraint. In the mean time every effort should be continued to quiet the delirium, and when the patient refuses to swallow, the drugs and nourishment should be administered by the rectum.

It is deemed appropriate to speak of the treatment of hemorrhagic smallpox under this head, for the peculiar manifestations of that type of the disease become strikingly apparent during the eruptive stage; and, moreover, it is rare for a well-marked case to live beyond the limits of the vesicular stage. Treatment is of little avail in this phase of variola. The remedies usually employed are acids, quinine, ergot, and tincture of chloride of iron; but these, we think, are prescribed more in conformity with general usage than with the expectation of obtaining any real benefit. When hemorrhage takes place in the various cavities or internal organs of the body, it is recommended that styptics be employed, together with injections of ice-water, or the use of cold compresses or tampons, although it is admitted that the beneficial effect of these agents is very slight. Transfusion and hypodermoclysis with saline solution have been tried, but have not given very encouraging results.

This type of the disease in varioloid is not quite so significant of danger as in variola. We have seen a few hemorrhagic cases of varioloid

in which the hemorrhage from internal organs was not very profuse or protracted, although the purpuric spots were well marked, recover under the free use of iron and stimulants. In these cases nourishment was freely taken, prostration was at no time profound, and, as the patients passed favorably through the eruptive stage of the disease, the petechiæ gradually disappeared and convalescence became established.

The most appropriate *diet* during the eruptive stage of variola is a liquid or soft diet. It should be easy of digestion and very nutritious, for the patient has yet to pass through a severe ordeal, in which his power of endurance will be tested to the utmost. Such articles as animal broths, milk, and eggs may be freely given. Bread may be added to the broths or to the milk, or it may be given in the form of milk toast. In varioloid, the appetite during this stage is often unaffected; such patients require but little treatment, and may be allowed almost perfect freedom in choice of diet.

4. Stage of Suppuration.—The indications for treatment during this stage are to mitigate the fever, to disinfect the exudation from the skin, to relieve the dangerous throat symptoms, and to resist by every possible means the tendency to death from exhaustion. If the patient's life can be prolonged through this stage, his chances for recovery increase with each succeeding day.

The febrile reaction which had abated considerably when the eruption first appeared, now increases to a notable degree, sometimes reaching a greater elevation than existed during the initial stage. In variola confluens the temperature at this period of the disease usually ranges from 103° to 106° F. Various drugs and other means have been employed for the purpose of reducing the intense heat of the body, but not one of them has given results entirely satisfactory. Quinine has been recommended, but in order to exert its antithermic properties it must be given in doses of 10 grains, repeated every half-hour or hour until 40 grains have been taken. This usually produces effects so unpleasant that we seldom give it in antipyretic doses. We use it, however, quite freely as a tonic, and also on account of its favorable action in preventing septicæmia. Some one of the antipyretics of the coal-tar series may occasionally be found useful. There is no doubt about the power of either antipyrin, acetanilid, or phenacetin to reduce temperature, but we do not feel sure that the use of these drugs in all cases is unattended with risk. However, when used carefully and in selected cases we do not think the risk is very great. We have found the administration of phenacetin in 2½ or 5 grain doses, when the temperature is high, to lessen the fever by one or two degrees, without producing any unpleasant effects.

BATHS.—Cool immersion baths, which have been recommended so highly in Germany for reducing high temperature in typhoid fever, have not met with anything like the same favor, even in that country, in the treatment of variola. Apart from the difficulty of getting a patient in the pustular stage in and out of the tub, it is found that they do not afford much relief. The use of cold compresses and of cold sponging are more easy of application and are very often serviceable. We have seen

patients temporarily benefited in warm weather by covering them with sheets wrung out of cold water, but usually this treatment is not well borne in cold weather. Kaposi recommends the use of compresses moistened with tepid water; the choice between the employment of cool or tepid water should depend largely on the season of the year, and the sensations and temperament of the patient.

Continuous warm baths are often of great value in the treatment of smallpox. In the early days of medicine baths were employed in this disease with the idea of hastening the appearance of the eruption. With this end in view Rhazes advised his patients to be kept in a kind of *balneum vaporis*. Hebra advised a special tub for treatment by continuous immersion. He had previously noted the good effects of this procedure in extensive burns and in certain cutaneous diseases. He remarks: "I have found by experience that persons may remain in a warm bath a hundred days uninterruptedly day and night, without injury to their health." His object in treating smallpox by this method was "by thoroughly soaking the pustules to favor the escape of their contents, and, at the same time, to prevent access of the air so as to render it impossible that any decomposition of the pus should take place."

Stokes¹ commends the use of the warm bath and presents the history of a medical student suffering from a confluent smallpox with hemorrhagic tendency, in whom this treatment was employed. The patient was immersed for seven hours and the procedure repeated on the following day. Stokes says: "That this gentleman's life would have been sacrificed but for the timely use of the bath, few who have had any experience in prognosis can reasonably doubt. He was in the condition of a patient every portion of whose skin had been burned and ulcerated. The pustulation was almost universally confluent; the purulent matter highly putrescent; the hemorrhagic state developed, and the nervous system suffering—in fact, he had every symptom of the worst putrid absorption."

We have employed the continuous warm bath in smallpox in a limited number of cases and have been favorably impressed with its therapeutic value. The cases in which it was tried were desperate types of confluent smallpox, and, although we were unable in several of the patients to save their lives, the baths conduced much to their comfort. A bath of 95° F. seemed to be capable of reducing a temperature of 104° to 100° or thereabouts and of maintaining the temperature at about this level. With the reduction of the fever, the pulse decreased in frequency and delirium was replaced by sleep. We kept one young man with a most severe type of confluent smallpox in a continuous bath for five days. On removing him from the tub to the bed at the end of this time his temperature immediately rose from 100° to 103° F. Life was prolonged in this case, but the systemic poisoning was too profound to permit of recovery.

¹ Some Notes on the Treatment of Smallpox, Dublin Journal of the Medical Sciences, 1872, vol. III.

Apart from the antipyretic influence of the continuous warm bath it tends to macerate the pustules, hastens the discharge of their contents, and thus lessens the liability to secondary pyogenic infections of the skin. We have found the ordinary ward tub with an adjustable cradle attachment admirably adapted for continuous baths. In winter hot water must be frequently added to keep the temperature up to the desired degree. When the temperature of the water falls below 92° or 90° F. the patient will usually complain of chilliness. The continuous bath treatment requires the services of a special attendant night and day.

During the suppurative stage of smallpox the vital forces of the patient are put to the severest possible test. The prostrating effect of the septic absorption from the innumerable pustules must be necessarily very great. Watson has estimated that the quantity of pus in the skin amounts to quarts; that this estimate is quite accurate is evidenced by the fact that we found the amount in a case of confluent smallpox, by actual computation, to be five quarts. So extraordinary a drain upon the system demands that the strength of the patient should be vigorously supported; otherwise, evidence of exhaustion soon becomes apparent.

The first evidence of flagging of the vital powers is often seen in the subsidence of the redness and swelling of the face and hands; the skin becomes pale, the pustules present a shrunken or collapsed appearance, and the pulse grows rapid and feeble. Other symptoms indicative of exhaustion are subsultus tendinum, general tremors, a dry tongue, and delirium. These are always indications for the most liberal use of stimulants and nutritious and easily assimilated food. It is wiser, however, not to wait until the vital energies begin to flag before resorting to supporting measures. As the patient approaches the suppurative stage his strength should be preserved by constant reinforcement so as to enable him to encounter the struggle that is to follow.

It is our practice to commence with stimulants and nutrients at the beginning of the suppurative stage or earlier when deemed necessary. The method of their employment is about as follows: To an adult patient suffering from the confluent variety of the disease we direct that there shall be given in each twenty-four hours not less than two quarts of unskimmed milk, two to four eggs, and six to twelve ounces of whiskey; the latter being given usually in the form of milk punch. The eggs should be well beaten and taken with the milk (a little salt being added), or they may be given in the form of egg-nog. It is important that the nutriment be given at short intervals, since patients can seldom take a large quantity at one time. It is also important that the stimulants and nutrients should be faithfully continued during the night, for many a prostrated patient has sunk beyond recovery between midnight and morning, for the want of these measures.

In selecting the diet and stimulants, we should, of course, take into consideration the condition of the patient's stomach. If that organ should be weak, or disinclined to receive in sufficient quantity the nutritive material just referred to, or if there should be a great repug-

nance to milk, as is sometimes the case, such articles as bouillon with eggs, well-prepared beef-tea, nutritious broths, and liberal amount of wine should be given instead. As a stimulant for patients in profound prostration, Curschmann recommends the Stokes cognac mixture:

R.—Cognac optimi,	
Aquæ destillatæ	ad ℥ssv
Vitelli ovi	No. 1.
Syrupi	℥vj.—M.

S.—A tablespoonful every two hours.

We would suggest that this preparation might prove more efficacious if repeated more frequently, or given in larger doses.

In the way of drugs, quinine in tonic doses—2 grains every three or four hours—is, we think, of service at this stage of the disease. Digitalis seems to be indicated at times to steady the action of the heart, but if there be evidence of collapse or cardiac failure, carbonate of ammonium should be given in addition to the alcoholic stimulants, together with strychnia hypodermically, if deemed desirable. Delirium, which is often most prominent during this stage, should be treated in the manner already described. No more medicine should be given than is absolutely necessary, for the *less the stomach is taxed with the ingestion of drugs*, and the more entirely it is given over to the work of *sustaining the vital forces of the body*, the better will be the chances of recovery.

When the bowels are constipated a mild laxative may be administered, or, what is preferable, a simple enema may be given.

5. **The Stage of Retrogression, or Stadium Exsiccationis.**—The stage of retrogression is characterized by drying of the pustules, lessening of the pain, diminishing of the swelling and redness of the skin and of the involved mucous membrane. The eyes again open, the nasal passages become more patulous, swallowing is less difficult, and the countenance, in favorable cases, assumes a brighter and more hopeful appearance. This stage in unmodified smallpox usually begins from the eleventh to the thirteenth day of eruption, and runs very gradually into the stage of convalescence. In cases somewhat modified it commences a little earlier. During the greater part of this period the same general treatment recommended for the preceding stage should be continued. When, however, the patient shows well-marked indications of improvement the quantity of stimulants may be gradually diminished, and such articles as corn-starch, milk-toast, soft-boiled eggs, cup custard, and the like may be added to the diet. Quinine and some ferruginous preparation, especially the tincture of the chloride of iron, are particularly valuable at this time.

It will occasionally be found necessary to administer remedies for the relief of the diarrhoea which may develop during the desiccative stage. The ordinary drugs employed for this purpose, opium, the astringent tinctures, bismuth, etc., will, in the majority of cases, succeed in quieting the bowels. Often, however, these remedies require to be given in full doses and frequently repeated.

Œdema of the feet and legs is not infrequently seen after severe

attacks of smallpox. In such cases there is always great exhaustion and the patient is generally anæmic. The latter condition is doubtless the cause of the œdema in the majority of cases. In the treatment of these cases iron in some form should be administered, and a roller bandage applied to the feet and legs. If the kidneys be diseased, they should of course receive appropriate treatment.

The various complications of smallpox, both medical and surgical, should be treated according to the most approved methods, it being borne in mind, however, that the patient is suffering from an exhausting disease and one that has severely taxed the integrity of the important organs and tissues. During the terminal stages of the disease, tonics, particularly those containing iron, quinine, and strychnine, will be found extremely useful. Stimulants, especially in the form of malt liquors, and a liberal and nutritious diet will aid in restoring strength and weight to the convalescent patient.

Liability of Error in Determining the Therapeutic Value of Measures Employed in Smallpox.—The legion of remedies and specifics of all kinds that have been advised and used in the treatment of smallpox bear eloquent testimony to their inability to fulfill the extravagant claims made by their several advocates.

The type of smallpox has been very considerably changed by vaccination. Where this agent does not confer complete immunity against variolous infection, it is still quite sure to exercise a more or less marked modifying influence over the disease, according as the period at which it was performed is near or remote. Cases of smallpox thus modified may assume various grades of severity, from the mildest possible form to that barely distinguishable from variola vera. But even where the protective influence of vaccination seems to be completely lost, there is often sufficient of this influence remaining to cause a slight abridgement in the course of the disease, and thus a severe case is often helped through to a favorable termination. It is therefore easy to understand how a certain drug, or some special method of therapeutics, may acquire an unmerited reputation in the treatment of postvaccinal cases of smallpox. In determining the value of any remedy in the treatment of this disease, conclusions should be drawn only from its employment in unvaccinated cases. Furthermore, the prevailing type of the epidemic should not be left out of consideration, for it is a well-known fact that a varying percentage of cases recover in different epidemics. Certain therapeutic procedures employed during mild epidemics may be accorded an entirely undeserved commendation and value. If, during the uniquely mild epidemic of smallpox that prevailed in many parts of the United States from 1898 to 1905, some special therapeutic agent had been advised and generally used, there would have appeared no more incontrovertible fact in the history of medicine than that this remedy was an invaluable specific in the treatment of smallpox. And yet the mildness of this widespread epidemic, with a mortality rate among the vaccinated and unvaccinated of about 2 per cent. (*i. e.*, during the first two years), was not influenced to any appreciable extent by any therapeutic meas-

ures. Such observations serve to point out the pitfalls into which the ultra-enthusiastic therapist may fall.

It must be reluctantly admitted that *there is as yet no treatment capable of exerting a material influence in either shortening or modifying the course of smallpox.* This statement must not be interpreted as an indication of therapeutic nihilism, for while we know of no measures of aborting or abridging the course of smallpox, we recognize the extreme usefulness of medicinal treatment directed toward the relief of the symptoms and the accompanying complications.

In the management of smallpox greater progress has been made in the direction of prevention than cure. Since the general introduction of vaccination, epidemics of this once widespread and dreaded scourge have greatly decreased in frequency and in fatality.

Unmodified smallpox has always been an extremely difficult disease to manage, and the treatment, of course, has varied greatly in different epochs of medical progress. It was the practice for centuries in the treatment of smallpox to repeatedly bleed, to purge, to blister, to apply heating lotions, to administer heating drinks, to cover the body with heavy bed-clothes, and to carefully exclude from the bed-room every breath of fresh air.

This heating method of treatment, which in the light of modern ideas appears almost barbarous, was supplanted by a directly opposed system, the "cooling regimen," inaugurated by the celebrated Sydenham, and employed with good results to the present day.

Red-light Treatment of Smallpox.—A form of red-light treatment of smallpox was employed by John of Gaddesden, in the fourteenth century, and doubtless before him by Arabian physicians; its object was to excite the skin and cause the elimination of the poisons of the blood. John of Gaddesden, though court physician, is said to have been "a very sad knave." Gregory wrote, in 1843: "What think you of a prince of royal blood of England (John, the son of Edward the Second) being treated for smallpox by being put into a bed surrounded with red hangings, covered with red blankets and a red counterpane, gargling his throat with mulberry wine and sucking the red juice of pomegranates? Yet this was the boasted prescription of John of Gaddesden, who took no small credit to himself for bringing his royal patient safely through the disease." Gregory significantly adds: "Let us then avoid the errors of our ancestors without reproaching them."

Picton,¹ Black,² Waters,³ Barlow,⁴ and others have employed various methods of excluding the actinic rays of light in treating smallpox.

Within recent years, Finsen, of Copenhagen, has strongly championed the red-light treatment of smallpox. The treatment is based upon the exclusion from the sick-room of the actinic or chemical rays of light by the use of red-colored screens of one material or another. Finsen, in summing up the cases treated by this method, chiefly by Danish and

¹ The American Journal of the Medical Sciences, 1882.

² Lancet, June 27, 1867.

³ Ibid., February 4, 1871.

⁴ Ibid., July 1, 1871.

Norwegian physicians, says that out of a total of 140 to 150 cases of smallpox in 1 case only was the method inefficacious.

In the winter of 1902 the writers treated two cases of variola in a red room specially arranged for the purpose, with absolutely negative results in both. One patient died during the suppurative fever, and the other was badly scarred.

Dr. Nelson D. Brayton, of Indianapolis, observed 300 patients treated in red-light wards, with results no different from those obtained in day-light wards. We seriously question the assertion that the exclusion of the actinic rays of light will prevent suppuration and scarring in severe smallpox in unvaccinated individuals.¹

Other Highly Vaunted Remedies.—We have tried a considerable number of remedies which have been highly recommended from time to time, but with results so discouraging as to lead to their abandonment. Some years ago the sulphocarbolate of sodium was lauded as an agent of particular value. We employed it in seven cases, giving it in twenty-grain doses every three hours. All of these patients died. To be sure, they were all severe cases—all of them confluent, and some malignant. But they certainly presented a class of cases in the successful treatment of which something more than the ordinary measures are required, which requirement is evidently not met by the antiseptic properties of the sulphocarbolate of sodium.

In a well-known text-book on cutaneous diseases it is stated that the internal administration of the hyposulphite of sodium is capable of favorably modifying and shortening the process of suppuration. We have given this drug in twenty-grain doses every four hours day and night in a dozen or more cases without observing the slightest influence upon the course of the disease.

We have used a sixteenth of a grain of bichloride of mercury in the tincture of the chloride of iron every four hours in scores of patients without noting any particular results therefrom. Even in the late stages these drugs do not seem to exert any influence in preventing the formation of boils.

The favorable reports of the use of brewers' yeast in furunculosis and allied conditions prompted us to test its value in the treatment of smallpox. We employed it in about forty cases, giving it in two-drachm doses every four hours, day and night. We were not able to observe any special influence from its use. Neither did it appear to prevent, to any appreciable extent, the development of boils and abscesses. And yet a French physician, who recently administered yeast in a few cases of smallpox (in patients who had been previously vaccinated) was encouraged to announce his belief that brewers' yeast given early might completely abort the suppurative stage of smallpox.

Besides the drugs mentioned we have administered a few other anti-

¹ Since writing the above we have noticed an article on "The Red-Light Treatment of Smallpox," in the *London Lancet*, July 30, 1904, by Drs. Ricketts and Byles. Thirteen cases of smallpox were treated in a thoroughly well-equipped red-light room. The writers conclude: "We cannot agree that the treatment has any of the merits which have been claimed for it."

septic remedies, such as salicylic acid, salicylate of sodium, and carbolic acid, but we cannot say that we have seen beneficial results from their use. With xylol—which, according to Zuelzer, coagulates the contents of the pustules and cuts short their development—we have had no experience. Others, however, do not seem to have obtained the encouraging results which were claimed for this drug.

Serum Treatment of Smallpox.—It would appear from experiments performed by Copeman, Chauveau, Béclerc, Chambon and Ménard, and others, that the serum of a previously vaccinated heifer is capable, on introduction into a second animal, of producing a certain degree of immunity against a subsequent vaccination.

Prompted by this result, Béclerc employed such a serum in the treatment of a woman suffering from smallpox. He injected the enormous quantity of one and a half litres, and believed that the serum produced a most favorable influence upon the course of the disease. Auché, of Bordeaux, and Landmann, of Frankfort, employed serum from persons who had passed through an attack of variola. The quantity of serum injected was necessarily small and no appreciable results were obtained. In this country the serum treatment has been tried by Kinyoun and by MacElliot, the former claiming a successful result.

The authors have used the serum of vaccinated heifers to a limited extent in the treatment of smallpox. With a view of proceeding cautiously, we injected only a small quantity (20 c.c.) into each of six patients. The serum was drawn from the calf twelve days after vaccination. In none of the patients was there any perceptible change in the course of the disease. One patient, a lad aged fifteen years, received the serum before the appearance of the eruption, on the second day of the initial fever, but the exanthem appeared and progressed in the usual manner. We had intended to continue the experiments, employing much larger quantities, but a large bottle containing 700 c.c. of carefully collected and prepared serum was accidentally broken, and subsequently our supply failed us.

Copeman says, in regard to this treatment: "It would seem probable that no really useful results are likely of accomplishment until we are in possession of some more satisfactory method of immunizing the system of the animal from which the serum is derived. Such a consummation can only be expected when further research shall have provided us with reliable methods for the ready cultivation outside the animal body of the microbe specific to variola."

Local Treatment.—The local use of antiseptics in variola has been favorably reported by various writers. Bianchi praises the results obtained from the following treatment: The patient is first bathed in a solution of 1:20 of boric acid, using with this bath antiseptic soap. During the course of the disease, baths in the boracic acid solution, or in a solution of corrosive sublimate 1:1000, are used every four hours. After each bath the patient is anointed with iodoform and vaselin, from 1 to 5:100, according to the severity of the case. When possible

the pustules are opened with an aseptic needle and their contents evacuated. The patient is then wrapped in aseptic linen, which is frequently changed. It is claimed by the author that this treatment notably diminishes the duration of the eruption, lessens the fever, prevents severe ulceration and scarring, and thus leads to rapid convalescence.

Similar results are alleged to have followed the use of baths containing *permanganate of potassium*, the salt being added until the water is of a rose-red color. Our experience with permanganate baths has been entirely unsatisfactory. The baths were given daily and, in some cases, twice daily from an early period of the eruption. They did not seem to exert any favorable influence upon the course of the eruption or the disease. Indeed, during the employment of this treatment our mortality was more than 50 per cent.

Looking back over the literature of the subject, we find that the antiseptic treatment of smallpox by means of external applications is nothing more than the revival of an old practice that was employed and abandoned many years ago. It is true that when these agents were used a half-century and more ago, it was not because they possessed antiseptic properties, for the germ theory was not then known; but ignorance of this fact certainly could have made no difference in the result. As long ago as 1843, Gregory wrote: "The latest mode of treating the surface during the maturative stage of smallpox is that of applying mercurial plasters containing calomel or corrosive muriate of mercury, or covering the whole surface with mercurial ointment. In the French hospitals at the present time the latter mode is in fashion. The reports which have reached us of its success, however, are not very flattering. I have seen all three plans fairly tried at the Smallpox Hospital. The ointment and calomel plasters were inefficient. The plaster of corrosive sublimate converted a mass of confluent vesicles into one painful and extensive blister, but I am still to learn what benefit the patient derived from the change."

When the eruption reaches the vesicular stage there is usually experienced considerable burning, particularly of the face, hands, and forearms. For the purpose of preventing or alleviating this symptom, some ointment or oily substance will be found useful. Vaseline containing about 3 per cent. of carbolic acid makes an efficacious ointment; or, if the odor of carbolic acid be objectionable, oil of eucalyptus or thymol may be substituted. A preparation which we have frequently employed is composed of equal parts of lime-water and olive oil, to which is sometimes added an antiseptic and perhaps a little cologne water. This is freely applied with a large camel's hair brush.

When the burning sensation and pain are severe there is perhaps nothing which gives so much relief as cold applications, such as cloths wet with cool water and spread over the face and arms. Curschmann believes that cold and moisture are the most efficient remedies for this condition. He says: "In severe cases the application of iced compresses to the face and hands, or to any parts where the eruption is abundant,

will diminish the severe pain, lessen the swelling and redness of the skin, and make the patient more comfortable."

Moore advises the application over the face of a "light mask of lint thoroughly soaked in a mixture of iced water and glycerin (a tablespoonful of the latter in an ounce of water) and covered with oiled silk."

The development of the eruption in the thick skin of the palms of the hands, tips of the fingers, and soles of the feet not infrequently gives rise to great pain. Cold applications or iced compresses may prove of service in this condition, although we think we have seen greater benefit follow the use of luke-warm hand and foot baths. The frequent application of flannel cloths wrung out in tolerably hot water, or the use of hot poultices, is often of great service.

The topical applications recommended for the pustular condition of the skin are numerous. To assuage the pain, burning, and itching, to correct the offensive odor, to guard against septicæmia, and to prevent pitting are the principal ends aimed at in the selection of these measures.

During the period of suppuration the sensation of itching is quite as intolerable as the pain, so that it is almost impossible for the patient to refrain from scratching. In consequence of this, or from other causes, the pustules become ruptured in many localities and their contents discharged. This purulent material undergoes decomposition and gives rise to a highly offensive odor. Remedies are demanded to relieve the itching and correct the odor. Antiseptic and antipruritic washes, such as carbolic acid (1:100), or corrosive sublimate (1:1000), may be employed for this double purpose. About the mouth, nose, and eyes a saturated solution of boric acid in rose-water may be freely used. We have frequently employed a 5 per cent. solution of either carbolic acid or Labarraque's solution, directing that both the patient and the bedding should be sprayed with this solution every two hours.

Very excellent results are said to have followed the use of an unguent composed of 100 parts of cold cream to 4 parts of salicylate of sodium. M. Dujardin-Beaumetz reports that this ointment, in his hands, has not only been successful in destroying the repulsive odor in severe cases of smallpox, but has actually prevented suppuration. In addition, he advises that a powder of 100 parts of talc to 6 parts of salicylate of sodium be dusted over the affected localities.

We have sometimes been able to lessen or modify the horrible odor by using as a dusting powder, subnitrate of bismuth, boric acid, and, sparingly, iodoform. To either of these, and especially to the latter, talc might be added. We have also derived advantage from a dusting powder composed of 15 to 20 parts of aristol to 100 parts of talc.

MacCombie strongly counsels the early removal of the crusts, which he asserts can best be accomplished by the use of a linseed-meal poultice, sprinkled with iodoform. "On the face the method most agreeable to the patient is to cut a mask of a single thickness of lint, with apertures for the nose, mouth, and eyes; then to smear a thin layer of linseed-meal poultice on this, taking care to put on the surface a little vaselin in

which iodoform has been mixed, and to apply this poultice to the face, changing it at least every two hours." (Moore.)

Various, indeed, are the methods that have been recommended for the *prevention of pitting in smallpox*, and yet we think it can be truly said that no one of them has stood the test of experience. From the unmodified form of the disease disfigurement is as great and as much dreaded at the present time as it was in the days of our ancestors, and it seems probable that this will continue to be the case until some agent is found capable of causing the eruption to abort before it reaches the pustular stage, for the suppurative process at this stage is attended with destruction of cutaneous tissue, and consequently scarring must follow. If any ectrotic measure were reliable, it would be easy by its employment to limit the amount of cutaneous inflammation and suppuration, to lessen, if not prevent, the so-called secondary fever, and thus obviate the danger from exhaustion. Hence, such a measure would serve the double purpose of preventing pitting and saving life.

Of the various ectrotic measures recommended we shall refer only to those which are spoken of most favorably. Opening the vesicles with a fine needle and evacuating the contents is a method advocated by Rayer and others. Also evacuation of the vesicles, followed by cauterization by means of a fine-pointed stick of nitrate of silver, has been highly recommended, especially by Velpeau, Bretonneau, and others. The exclusion of light and air from the skin is alleged to prevent pitting. The Egyptians and Arabs sought to accomplish this by covering the face with gold leaf; and others, more recently by covering the face with certain dark-colored plasters, and by employing red light. Collodion has had its advocates, and a solution of gutta-percha in chloroform has been recommended by such authorities as Stokes, Graves, and Wallace. In using either of the two latter preparations it is advised that they be applied to the face once or twice daily with a camel's hair brush, and that the applications be commenced while the eruption is papular, or while vesicles are quite small. These agents are supposed to act by excluding the air and by mechanical pressure.

Tincture of iodine, applied in the same way and at the same period of the eruption, has been highly recommended. Sargent is said to have tested the ectrotic power of this agent in thirty cases of smallpox, the application being limited to one side of the face. According to the description given of the results, there was not so much swelling where the iodine was applied, the vesicles were flattened, and while the pitting was not prevented it was perceptibly diminished. Lemaire and Sansom claim to have used successfully carbolic acid diluted with alcohol. This was applied as soon as the vesicles began to assume a purulent form. Certain merit has been claimed for subnitrate of bismuth and prepared chalk, in equal parts, when applied twice daily in connection with sweet oil. Sulphur ointment (from 1½ to 2 drachms to 1 ounce of lard), rubbed lightly over the affected parts three times daily, has been recommended as useful in preventing suppuration of the vesicles, and thus saving the skin from disfigurement.

Mercury has, perhaps, been more highly praised than any other ectrotic remedy. It has been employed in different forms, both as a plaster and as a wash. M. Briquet was in the habit of using a mask composed of mercurial ointment and sufficient powdered starch to solidify the mass, so that it could be moulded to the various parts of the face. He renewed this application once or twice a day. The French physicians have been very partial to a compound mercurial plaster, known in the French Pharmacopœia as "plaster of Vigo." It has been claimed that if this plaster be applied over affected surfaces before the fifth day of the eruption, the papules either disappear by resolution or change into vesicles or tubercles. According to M. Briquet, the latter change seldom takes place except upon the face. It has been recommended that the plaster be kept on from eight to twelve days. When removed it is said that only small, hard excrescences are seen, and that these disappear in ten or twelve days without leaving any scars. It is admitted that pyalism has been known to occur from the use of this plaster. Hence, Bennett was led to substitute for the mercurial plaster calamine saturated with olive oil, which he found effective. A solution of corrosive sublimate (1 grain to 6 ounces of distilled water, with 1 drachm of laudanum) applied by means of compresses, is said to have caused the pustules to disappear without much ulcerative action. This application was recommended and used nearly fifty years ago. More recently Niemeyer recommended the employment of a solution of about the same strength (corrosive sublimate 1 grain to water 6 ounces). Skoda and Hebra advised that the compresses be dipped in a much stronger solution (grains ij-iv to water ℥vj). Still other measures have been highly lauded for this purpose, but we shall not consume time and space by referring to them.

The results which, in our experience, have followed the use of the so-called ectrotic measures have by no means been encouraging. Perhaps one-half of our patients have recovered from smallpox without permanent scarring, but the result in these cases would have been the same if simply lard or cold cream had been applied to the face, or, indeed, if no application at all had been made. In the severe confluent cases, no remedy has been successful in preventing pitting, although we have tested practically all of the more highly recommended measures.

We feel strongly inclined to agree with Gregory, who said: "There is no peculiar method which can be devised for the prevention of pits and scars. The masks and ointments formerly in use for that purpose, and so highly vaunted, are, in reality, more hurtful than beneficial. The application of a little cold cream to the hardened scabs is all that can be recommended."

We have had the skin in the papular stage of the eruption thoroughly washed with soap and water, alcohol and ether, and bichloride of mercury, and then covered with ichthyol-collodion, the last-named application being applied twice a day. This antiseptic treatment did not seem to interfere in any way with the formation of the pustules, for they grew up through the ichthyol varnish.

The remedy which appears to have accomplished most in our hands is the *tincture of iodine*. We do not make the extravagant claims for this application that some writers have done, but we do think that it has been a little more useful than anything else that we have employed. Our habit has been to paint the face as early as possible with the undiluted tincture of iodine and to continue the application once or twice a day according to the sensitiveness of the skin. Most patients bear the painting very well, although many complain of smarting for a time after the treatment. In some patients the skin is so sensitive that this mode of treatment has to be abandoned, although a tincture of one-half the usual strength might be applied in such cases. About the eighth to the tenth day of the eruption, in unmodified cases, a thin, dry, parchmenty mask is formed which begins to crack and peel off. At

FIG. 58



Showing the effect produced by painting the right arm from the elbow to the wrist daily with tincture of iodine. Area painted is free of the secondary impetigo sores seen upon the untreated arm. Left arm was not painted.

this time it will be found advisable to substitute an unguentous application. We believe that the iodine treatment tends to shrink the pustules, to hasten decrustation, and, to some extent, to lessen the pitting, although in severe cases it will not prevent it. The liability to consequent pyogenic complications of the skin appears to be diminished. A notable feature of this treatment is that it completely destroys the offensive odor arising from the areas of skin to which the iodine is applied.

We have also obtained good results from mild emollient ointments, with or without antiseptic ingredients. We are not sure that any special combination is essentially more useful than plain petrolatum or cold cream. In the early stages of the eruption, these applications are quite grateful to the skin, and later on they serve to soften the purulent

debris, which can then be more easily removed from the face. In some cases, where the treatment of the face is neglected, the odor is more offensive, and the ulcerations appear to be deeper and followed by more disfiguring pitting.

We have frequently incorporated carbolic acid, aristol, bismuth of mercury, etc., in the ointments applied. As above stated, however,

FIG. 54



Smallpox eruption at a late stage showing extensive dark crusting on the face resulting from neglect of local treatment.

these did not seem to materially increase the efficiency of the applications. To soften the crusts from the skin, nothing is better than a salve of the following composition:

℞—Sodii bicarbonatis 3℥.
 Petrolati q. s. ad 3℥.

We have found great benefit to result from the use of baths given during the stage of pustulation and desiccation. These may be made

antiseptic by the addition of creolin (1:500) or bichloride of mercury (1:10,000 to 1:20,000). The purulent accumulations and crusts are detached from the skin by the baths, and the associated septic fever is greatly lessened. Furthermore, the liability to pyogenic skin complications is diminished. When it is inconvenient or impossible to employ antiseptic baths, much good will often be derived from opening and evacuating the pustules, and washing the bases with absorbent cotton saturated with a 1:5000 solution of bichloride of mercury.

When extensive impetigo exists we employ a bichloride bath and then dust the patient with a weak aristol or iodoform talcum powder. An ointment which will be found useful in treating impetigo pustules is:

℞—Hydrargyri ammoniati gr. x.
 Pulv. amyl.,
 Pulv. zinci oxidī āā 3ij.
 Petrolati 3ss.

Treatment of Eye Complications.¹—The air in the sick-room or hospital ward should be changed as frequently as possible. The hands of the patient should be encased in gloves or protective bandages to prevent contamination of the eyes. As a matter of daily routine the eyes should be flushed copiously with warmed, weak, salt or boracic acid solutions. The edges of the eyelids should be anointed with vaselin. In all examinations of the eyes great care must be used in the manipulation, lest the cornea be injured.

In the early stages, when the eyes are hot and flushed and feel heavy, a douche or spray of ice-cold water often brings relief. In excessive hyperæmia, frequent bathing with water as hot as can be borne will have a soothing effect. In other cases, cloths saturated with lead-water and laudanum, or ice-cold compresses may be laid upon the closed lids.

The conjunctival sac should be frequently flushed with warm boracic acid solutions. At bed-time the edges of the lids should be anointed with vaselin, or with yellow oxide of mercury in vaselin, 1 grain to the drachm, to prevent their becoming glued together.

When conjunctivitis sets in with a mucous or mucopurulent discharge, mild astringents should be used; saturated solutions of boracic acid, to which may be added a few grains of sodium chloride, can be employed. The lids are to be inverted and the mucous surfaces painted with weak solutions of silver nitrate (1 to 5 grains to the ounce) or protargol in 5 to 10 per cent. solution may be satisfactorily employed. In some instances the discharge may be so free that stronger astringents must be used. Here no more efficient remedy than silver nitrate can be applied, for in its action it is germicidal as well as caustic. When the lids are tense and board-like, however, and their mucous surfaces covered with a gray film or false membrane, it is not to be used; but only when the lids are relaxed, the discharge creamy, the conjunctiva

¹ The chapter on the Treatment of Eye Complications has been kindly prepared for us by Dr. Burton K. Chance, whom we have frequently called in consultation to advise us in the treatment of severe ocular lesions at the Municipal Hospital.

red, and the retrotarsal folds puckered. After thoroughly cleansing them the conjunctival surfaces should be brushed daily with strong silver solution, 10 to 20 grains to the ounce; the excess of the drug is to be washed away by an abundance of common salt solution.

These washings are to be repeated until the membrane is clear and red, and as long as the discharge is abundant the use of silver is indicated.

The edges of the lids are to be greased with vaselin, and they are then to be restored to their normal position. The pressure on the globe, caused by the swollen lids may be so great as to necessitate the cutting of the outer canthus. A canthotomy may have to be done also to facilitate the examination of the conjunctiva and the cornea.

Persistent and increasing chemosis of the conjunctiva demands snipping in order to relieve the pressure on the cornea.

When the lids are tense and the secretion flocculent, the local application of cold is most useful. The readiest means of applying it is as follows: Small squares of lint of several thicknesses of gauze are placed on a block of ice. When these are cold the excess of water is squeezed out from them and they are laid on the swollen lids. They must be changed sufficiently often to maintain a uniform coldness. In some cases it may be necessary to apply them continuously, while in others they need be used for short periods only several times a day.

When the *cornea* is involved great care must be exercised during any manipulation, lest pressure be exerted on the globe.

Efforts at cleanliness must be redoubled. Solutions of atropine of four grains to the ounce are to be used twice or thrice daily, to effect complete mydriasis, when the ulceration is central. But if the ulceration be marginal eserine salicylate in weak solution, one-quarter grain to the ounce, may be used, but with great carefulness, as this drug is liable to increase the hyperæmia of the iris, with consequent iritis. Therefore, the use of this drug should be discontinued when the pupil has become contracted. Ice must be discontinued and hot compresses are to be substituted. Squares of gauze wrung out of water which is kept at about 110° F. are to be frequently applied.

Every attempt should be made to remove all of the discharges and to restore the conjunctiva to its normal condition. The lids are to be separated very gently and all of the tenacious secretion is to be wiped off with swabs of cotton. The conjunctival sac is then to be flushed with warm boric solutions. This attention should be given every hour, or, if necessary, at even shorter intervals. Although other stronger antiseptics may be tried, we are of the opinion that the careful and persistent use of mild boric acid or weak bichloride of mercury solutions should yield the best results.

Where *perforation of the cornea* is threatening, the edges of the ulcer must be cauterized at once. Here a dull hot probe, thoroughly applied, may end the process. We have used, besides the hot probe, solutions of carbolic acid, of iodine, and crystals of trichloroacetic acid. If there

be not too much conjunctival secretion, a well-applied roller bandage may afford the proper support to the already weakened corneal membrane.

A low grade of conjunctivitis may persist for a week or even months after convalescence from smallpox in persons whose illness has been complicated by serious conjunctival inflammation. Here the use of stimulating astringents like the boroglyceride or the glycerole of tannin act with signal advantage. Argentamin, 2 to 5 per cent., or largin, 5 to 10 per cent., may be tried.

Formalin, 1:5000, or bichloride of mercury, three-quarters of a grain to the pint, may be used with success in more severe cases with considerable discharge.

CHAPTER VI.

CHICKENPOX.

Synonyms.—*Varicella*; formerly, *Variola crystallina*, *Variola natha*, *Variola spuria*. English, formerly, *water pock*, *glass pock*; German, *Varicellen*, *Wasserpocken*, *Wind blättern*, *Schafpocken*; French, *la varicelle*, *la vérolette*; Italian, *Merrighione*, *ravaghione*.

Definition.—Chickenpox is an acute, highly contagious disease, occurring chiefly in children, characterized by an eruption of vesicular type, appearing in crops and accompanied by mild febrile disturbance, which usually begins with the appearance of the cutaneous outbreak. The lesions dry in a few days into crusts. One attack protects for life in the vast majority of cases.

History.—Chickenpox is doubtless a disease of great antiquity, although for centuries it was confounded with smallpox. The Arabian physician, Rhazes, who lived in the ninth century, made mention of a mild or spurious eruption which was not protective against epidemic smallpox. The Sicilian physician, Ingrassias, seems to have been the first to have described varicella in accurate terms; this appeared in a work entitled *Praternatural Swellings*, written in 1553. Vidus Vidius, an anatomist and physician, wrote some forty years later, employing for varicella the term *crystalli* or *variola crystallina*, a designation which clung to the disease for many years.

Sydenham makes no mention of the disease. An admirable description, which admits of no room for doubt, has come down to us from the pen of Riverius, who wrote in 1646.

Morton's writings on the subject are of historical value, because, according to Gregory, he remarks that the disease was vulgarly known as *chickenpox*. This appears to be the first mention of this term in literature. The name *chickenpox* is said to be derived from the word *cicer*, a chicken-pea, the French word for the same being *chiche*. Morton (1694) referred to varicella under the title *variola admodum benigna*, regarding the disease, as did all of his contemporaries, as a variety of smallpox. In 1696 Harvey contributed some important writings on the subject.

Although the credit of recognizing the duality of chickenpox and smallpox is commonly given to Heberden, it in reality belongs to Fuller, who, in 1730, expressed his views in the following interesting language: "The pestilence can never breed the smallpox, nor the smallpox the measles, nor they the crystals or chickenpox, any more than a hen can breed a duck, a wolf a sheep, or a thistle figs, and therefore one sort cannot be preservative against any other sort."¹

¹ Quoted by Gee, Reynolds' System of Medicine, American edition, 1879, p. 124.

In 1767 Heberden contributed to the first volume of the *Transactions of the Royal College of Physicians* a carefully prepared thesis in which he urged the dissociation of smallpox and chickenpox. He employed, however, the unfortunate title of *variola pusillæ*, ignoring the term *varicella* which had been introduced a few years before (1764) by Vogel in Germany. His work, though at first strongly criticized, became for many years the acknowledged classic on the subject. The term *varicella* is a diminutive for *varus*, a pimple.

In Germany, Sennert in 1676 was the first writer to call attention to *varicella*. In Holland, Diemerbroek was the physician to achieve this distinction. In the following century the most important literary contributions were made by Frank, of Vienna, in 1805; Willan, of London, in 1806; Heim, of Berlin, in 1809; and Möhl, of Copenhagen, in 1817.

In 1820, Thomson, of Edinburgh, obscured the comprehension of the disease by reasserting the old doctrine of the identity of *variola* and *varicella*, thus leading medical opinion into one of those by-paths which so constantly cross the road of medical progress.

And again in 1866 there appeared a champion of the doctrine of unity, in no less a person than Ferdinand Hebra, the great Viennese dermatologist. Hebra regarded *varicella* as a mild form of smallpox. He wrote: "I apply, then, the name *variola vera* to the most severe form of this disease, that in which the eruption is abundant and the fever intense, and in which a fatal result is often observed. On the other hand, I use the term *varicella* for cases in which the rash is very scanty and which run a favorable course and always terminate in recovery." And, again, "There is positive proof that *varicella* may generate *variola* or *varioid*, and, conversely, *variola* may produce in another individual *varicella*."

When it is remembered that mild cases of smallpox were regarded by Hebra as *varicella* the above statements need occasion no surprise. It is difficult to conceive, however, how a close observer like Hebra could have convinced himself that there was no chickenpox distinct from smallpox. Hebra's large experience in smallpox and his fame as a teacher led to an acceptance of his views in many quarters. Curschmann, writing in 1875, says: "Concerning the relation of *varicella* to *variola*, no perfect unity of opinion has yet been reached. While Hebra's view of the close connection of the processes was universally respected until a short time since, and has its supporters even at the present day, authoritative voices are again raised in favor of their separation."

Hebra's views were taught by his successor, Kaposi, until his death a few years ago. Kassowitz, of Vienna, has also tenaciously adhered to the view of the identity of smallpox and chickenpox.

It is remarkable that a proposition so readily capable of proof as the distinctiveness of smallpox and chickenpox should be repudiated by such eminent teachers and observers. The chief explanation of the astounding assertions they make is the unwarranted use of the term *varicella* to designate very mild cases of infantile smallpox. This and

the failure to recognize chickenpox as a separate disease account for the discrepancies of these observers as compared with the almost universal teaching.

With these few exceptions, physicians throughout the world are agreed that chickenpox is a distinct disease having no relationship whatsoever to smallpox.

It would be an act of supererogation at the present day to produce the evidence in support of the duality of these two diseases.

ETIOLOGY.

Age.—Chickenpox is essentially a disease of early childhood. It is most common between the ages of one and seven years. Although it develops at times in infants at the breast, they more commonly escape the infection when exposed to it. The statement made by many authors that chickenpox is excessively rare in adults requires qualification; this view has been so commonly held for many years that we have deemed it advisable to discuss the subject of adult varicella under special caption. We have within a few years seen two score or more cases of chickenpox in adults, and similar experiences have been recently reported by others. The most advanced age at which we have seen the disease is forty-nine years. The youngest period at which varicella appears to have been observed is recorded by Senator, who saw an infant of eleven days with the disease.

The following table, compiled by Gee¹ from the records of the Children's Hospital of London, shows the age incidence among children:

	Boys.	Girls.	Total.
Under 1 month	2	0	2
" 2 months	2	6	8
" 3 "	4	9	13
" 6 "	29	23	57
" 12 "	45	52	97
" 18 "	34	28	62
" 2 years	36	39	75
" 3 "	38	42	78
" 4 "	47	58	105
" 5 "	44	62	96
" 6 "	33	25	58
" 7 "	19	11	30
" 8 "	10	19	29
" 9 "	4	6	10
" 10 "	3	2	5
" 12 "	1	6	7
	349	378	727

Varicella prevails more at certain times than at others and may occur in epidemics. In large centres of population, however, the disease is like scarlet fever, endemic, and to a certain extent always present. The mildness of chickenpox favors its dissemination, inasmuch as children frequently attend schools while still in an infectious state.

¹ Loc. cit.

Susceptibility is not influenced by race, the negro and the Caucasian taking the disease with equal facility. Neither does varicella seem to be influenced by climate or season.

While varicella is extremely contagious, its infecting power is not as intense as that of measles or smallpox, and it is an easier disease to control by isolation. As far as we know, the infection gains entrance to the individual through the respiratory tract. In the vast majority of cases chickenpox is contracted by direct exposure to a person suffering from the disease. It is not impossible that the affection may be carried by a third person or through the agency of infected objects, but this is in all probability uncommon. It is possible for the disease to be transferred before the appearance of the eruption; this is exemplified in the following case:

A physician's daughter, aged sixteen years, developed a slight sore throat and a little fever, and was isolated in a room in the upper story of her home. A small, whitish patch was noticed on the posterior pharyngeal wall. On the following day the eruption of chickenpox appeared. An eight-year-old brother who was with the patient on the previous day was kept in a distant part of the house, out of all communication with the sister or her attendants. Sixteen days after exposure, the same having taken place before the appearance of the eruption, the boy developed chickenpox.

It is not surprising that varicella should occasionally be communicated before the appearance of the cutaneous outbreak, when we remember that smallpox may be transmitted during the initial stage of the disease.

How long a patient remains capable of transmitting the infection has not been definitely determined. Nor is it known whether the infective agent is present in the crusts, as is the case in smallpox. In the absence of positive knowledge on this point, it is wise, in order to prevent contagion, to isolate the patient until the skin is entirely free of the original crusts. Crusts due to secondary infection of the skin are not capable of transmitting the disease.

Second attacks of chickenpox are of great rarity. Thomas never observed a second attack, an experience which corresponds with ours. Gerhardt is said to have treated a child with three attacks, and a similar observation is recorded by Heim. Vetter states that he saw the child of a physician who had two attacks of chickenpox within fourteen days. Neale¹ reports a second attack of varicella after an interval of ten days. Trousseau, Boeck, Kassowitz, Hufeland, and Canstatt have also reported cases. These isolated instances do not, however, controvert the general experience of physicians that one attack of chickenpox, in the vast majority of instances, protects against future attacks.

Inoculability of Varicellous Fluid.—Numerous investigators have endeavored to determine whether varicella can be communicated by inoculation. Willan believed that the disease could be thus trans-

¹ *Lancet*, 1891, ii.

mitted, but Gregory remarks that "his experiments are few and, to my mind, unsatisfactory." Bryce, of Edinburgh, in 1816, made extensive trials, with negative results. He states¹ that he has inoculated with the fluid of varicella vera, at all periods of the disease, and at all seasons of the year, children who had never undergone either smallpox or cowpox, and yet he had never been successful in producing from it either variola or varicella.

Delpech, in 1843-44, attempted to inoculate patients with varicella at the Hospital Necker in Paris, but with unsuccessful results.² Hessa³ compiled data of 113 inoculations with varicellous fluid; in 87 of these no result was obtained, in 17 there was merely a local manifestation, and in 9 cases a general eruption ensued. Thomas obtained negative results in his inoculations and mentions the fact that Heim, Vetter, Czaker, and Fleischmann had similar experiences. J. Lewis Smith in this country likewise failed in his attempts to transfer chickenpox to children who had never had the disease.

Steiner⁴ obtained results very different from those above referred to. He claims to have inoculated ten children, eight of whom developed typical chickenpox. The time elapsing between the inoculation and the appearance of the eruption in these cases was eight days.

If the possibility of transmission of the disease in the usual manner was entirely excluded in Steiner's cases, his observations go very far toward proving that chickenpox can be communicated by inoculation. In view, however, of the negative results obtained by nearly all other investigators, future experiment will be necessary to confirm the successful inoculations obtained by Steiner.

Period of Incubation.—The stage of incubation of chickenpox is ordinarily longer and more variable than that of smallpox or measles. Different observers assign rather variant limits to this period, as will be seen by reference to the following quotations:

Gregory⁵ says "it does not exceed four days and is certainly less than a week;" Heberden⁶ places it at eight or nine days; Trousseau,⁷ "fifteen to twenty-seven days;" Gee,⁸ "at about a fortnight;" Thomas,⁹ thirteen to seventeen days; Delpech, twelve days; Holt,¹⁰ "quite uniformly from fourteen to sixteen days;" Corlett,¹¹ ten to nineteen days.

Our experience would lead us to regard fourteen to seventeen days as the usual period, although we have observed it to extend over nineteen days and even as long as twenty-one days. It is possible that in rare cases it may be less than ten days and longer than three weeks.

In 16 cases occurring in an outbreak in the Municipal Hospital we

¹ See Thomson on Varioloid Diseases, p. 74, quoted by Gregory.

² Quoted by Gregory.

³ Ueber Varicellen, Leipzig, 1829.

⁴ Wiener med. Wochen., 1875, No. 16.

⁵ Lectures on the Eruptive Fevers. First American edition, 1851, p. 295.

⁶ Quoted by Gee. Loc. cit.

⁷ Lectures on Clinical Medicine. American edition, Philadelphia, 1882, p. 136.

⁸ Reynolds' System of Medicine. American edition, Philadelphia, 1879, p. 125.

⁹ Ziemssen's Encyclopedia of Medicine.

¹⁰ Diseases of Infancy and Childhood, p. 929.

¹¹ Acute Infectious Exanthemata, p. 165.

PLATE XXXVIII.



Chickenpox Vesicles Surrounded by Reddish Areolæ.

were able to fix the incubation stage quite accurately. The periods were as follows:

13 days in	.	.	1 case.	18 days in	.	.	1 case.
14 "	.	.	7 cases.	19 "	.	.	1 "
15 "	.	.	3 "	21 "	.	.	1 "
17 "	.	.	2 "				

Steiner, who claims to have successfully inoculated varicella in eight patients found the incubation stage in these patients to be uniformly eight days. During the incubation period there are, as a rule, no evidences of disturbed health. Now and then, however, as in some of the other exanthemata the breeding of the disease may give rise to slight symptoms, such as loss of appetite, lassitude, and general indisposition.

SYMPTOMATOLOGY.

Pre-eruptive Stage.—In the vast majority of cases chickenpox is not preceded by a prodromal illness. The onset of the constitutional manifestations is usually coincident with the appearance of the eruption. The ordinary history elicited from mothers is that the eruption is the first symptom to attract their attention, and that the children are not ill prior to this time.

At the Municipal Hospital we have had the opportunity of studying the temperature records of a number of chickenpox patients before the appearance of the eruption; these patients were convalescent from scarlet fever when they developed varicella. In almost every instance the temperature remained about normal until the chickenpox eruption appeared and, indeed, in some cases even after the lesions had developed.

In a small percentage of cases some little constitutional disturbance may be observed a day or two before the appearance of the exanthem. This consists of slight rise of temperature, anorexia, vague pains, and chilliness. More common is it to discover these symptoms a half-day or so before the eruptive outbreak. During the night preceding the appearance of the exanthem the child may be slightly feverish and restless. But these mild precursory symptoms should not be regarded as representing a prodromal illness, for by this term as applied to smallpox is meant a distinct stage preceding by two or three days the onset of the eruptive phenomena.

It is important, however, to call attention to the fact that varicella in adults may occasionally be preceded by a prodromal stage. While most of these patients give no history of a pre-eruptive illness, a minority of them will volunteer such information. We have seen perhaps a half-dozen of adults suffering from varicella who had distinct prodromata. These symptoms consist usually of chilliness, lassitude, anorexia, nausea, slight headache and backache, and some elevation of temperature (101° to 102° F.). These manifestations may precede the appearance of the eruption by two or three days, though more often not longer than twenty-four hours. It is rare to observe high fever, vomiting, severe lumbar pain, and prostration—symptoms which usher in a well-pronounced smallpox.

In general, it may be said that a true prodromal stage in children suffering from chickenpox is extremely rare; in adults it is by no means so infrequent. When it does occur it is much milder than the prodromal illness ordinarily observed in smallpox. A *prodromal erythema* is, in rare cases, seen before the appearance of the varicellous eruption, as it is at times before the eruption of smallpox and measles.

Thomas observed "just before the outbreak of a light case of varicella with ephemeral though intense fever (105.8° F., rectal temperature) the appearance of a universal erythema of short duration." He adds, however, that although he watched carefully for these eruptions this was the only one he ever saw.

Henoch is also said to have seen and described such an erythema.

A prodromal scarlatinoid rash preceding the appearance of the varicella eruption was observed by us in a patient admitted into the scarlet-fever ward of the Municipal Hospital in the early part of 1902. A girl, aged five years, was sent to the hospital from a large foster home. She had had vomiting, some elevation of temperature, and on admission there was a diffuse scarlatiniform rash covering the entire trunk. This resembled scarlet fever so strongly that an experienced interne regarded it as the scarlatina exanthem. The rash faded in the course of twenty-four hours and was followed by the appearance of a number of varicella vesicles. At the end of five days after admission to the ward, a rise of temperature to 103° F. occurred, accompanied by sore throat and a well-pronounced and typical scarlet-fever rash. It was evident that the child contracted scarlet fever in the ward. No scarlet fever existed in the foster home from which the child was received.

The Eruptive Stage.—As has been stated, the eruption is commonly the first symptom to attract attention to the disease. Synchronously with the appearance of the cutaneous outbreak, or a few hours before or afterward, a varying degree of fever sets in. In some cases this does not reach higher than 99° F.; in others, however, the pyrexial elevation may be most marked. Thomas records one case in which the initial temperature was 105.8° F., and we have on several occasions observed temperatures of 104° and 105° F. This high fever is, as a rule, of brief duration, subsiding in twelve or twenty-four hours to 99° or 100° F. High fever does not necessarily presage the development of a profuse eruption. We have seen a temperature of 104° in a case with scant and abortive lesions.

The temperature commonly falls to normal in the course of one to three days. Where the eruption is copious, however, moderate fever may persist for four or five days. In cases in which the varicellous lesions become secondarily infected, the temperature may continue above normal for a fortnight or even longer.

The Eruption.—The eruption of chickenpox usually appears first on the back or the face, although other regions may be the seat of the initial lesions. Irregular extension then occurs, new lesions developing on different portions of the cutaneous surface. The hairy scalp is nearly always beset with some vesicles.

PLATE XXXIX.



Well-marked Chickenpox Eruption, showing Crusted Lesions and Recent and Old Vesicles. Fourth day.

The *distribution* of the eruption is subject to some variation, but is tolerably uniform in the majority of cases. The trunk, particularly the back, is relatively more profusely attacked than the distal portions of the extremities—the wrists, ankles, hands, and feet. The face usually presents a moderate number of discrete vesicles. It is rare for the face to escape completely, although at times but two or three lesions may be present. At other times, in copious eruptions, quite an abundance of lesions may be seen on the face. The arms and legs are seldom profusely attacked except in unusually extensive cases.

It has been claimed by some writers that varicellous lesions do not occur upon the palms and soles. It is true that in most cases the palmar and plantar surfaces are free of eruption; but it is by no means rare

FIG 55



Chickenpox lesions in the crusted stage, about the fourth day of the disease.

to find a few vesicles in these regions, and in severe cases the lesions may be fairly numerous.

The palms and soles are much less frequently and less abundantly involved than in smallpox, in which disease some lesions are nearly always present in these regions. The dorsal surfaces of the hands and feet are likewise relatively lightly affected compared with the general extent of the eruption. In fact it may be stated that the distal portions of the extremities usually suffer but little in chickenpox; the eruption prefers the covered surfaces.

The distribution of the eruption may, to some extent, be influenced by irritation of the skin prior to the appearance of the lesions. We have seen a profuse crop of lesions develop over a rectangular area on the sternum to which a mustard plaster had been applied during the pre-eruptive period. Any irritant by increasing the vascularity of

the skin may attract lesions to the region thus irritated. It is not so common, however, to observe an increase of the eruption from this cause as it is in smallpox. In the latter disease the influence of cutaneous congestion in determining an increase of the eruption in a given area is emphasized by frequent experience.

Usually by the time that the physician is called to see a child with chickenpox vesicles are observable upon the body. If the skin is examined early it will be noted that the vesicles are usually preceded by erythematous spots. These are pea to bean sized, rosy color, and in appearance not unlike the rose spots of typhoid fever, or fleabites. Very soon the centres of the macules become raised and small vesicles are formed which rapidly increase in size. In some cases the rosy macules are elevated, somewhat acuminate, and in fact represent papules.

The duration of the transitional lesions before vesiculation takes place is extremely variable. At times some of the lesions of varicella remain in the macular or papular stage and never go on to the development of vesicles. Indeed, Thomas mentions a case, the nature of which was due to the previous occurrence of varicella in a sister, in which the roseolæ (roseolæ) persisted for thirty-six hours and then without the formation of any vesicles whatever. Varicella without development of vesicles must, however, be extremely rare. Varicellous vesicles may spring up so rapidly that they appear to arise directly on the normal skin. We were enabled to determine in one instance that vesicles developed in less than four hours. A trained nurse bathed a child at 11 A.M. and carefully examined the skin for an eruption without discovering any. At 3 P.M., four hours later, we examined the child and found several fully formed, tense, varicellous vesicles on the trunk.

The lesions often look as if they had been produced by drops of scalding water sprinkled upon the skin. They are superficially situated, differing in this respect from the deeper-seated vesicles of smallpox. The epidermal roof of the vesicle is thin and readily ruptured.

The vesicles of chickenpox vary greatly in size; they may be no larger than a pinhead, or they may reach the dimensions of a large pea. They are commonly tense, although rarely as hard as the variolous vesicle. Slight traumatism, such as is produced by scratching or the friction of clothing, suffices to rupture the vesicle. The fluid from an early vesicle is clear and watery in appearance; later it becomes turbid or lactescent. The vesicles are round or oval, the shape being somewhat determined by the lines of cleavage of the skin. In the axillary and lateral costal regions they are commonly oval, the long axis corresponding with the direction of the ribs.

Chickenpox vesicles are commonly surrounded by a reddish areola. This may be narrow, measuring but an eighth of an inch; in other cases, however, it may have a breadth of a half-inch or more.

Much diagnostic value has been attributed by some observers to the comparative degree of evacuation of chickenpox and smallpox

PLATE XL.



A Severe Attack of Chickenpox, showing Lesions in Various Stages of Development (fourth day). Relative sparsity of lesions on the face as compared with the trunk.

vesicles effected by puncturing them with a needle. While it is true that the varicella vesicle is often completely emptied, and the variolous vesicle, owing to its more multilocular structure, less completely evacuated, but little value should be placed upon this test. There is too much latitude possible in the interpretation of the degree of evacuation effected.

The eruption of chickenpox appears in *crops*. The first outbreak commonly consists of a dozen to fifteen lesions. After an interval of some hours, usually a day or so, a second crop appears which often numerically exceeds the first. Twenty-four hours later a third outbreak may occur and new lesions may thus continue to appear for four or five days or even a week. Owing to the fact that the lesions are of different age, they are seen in varying stages of evolution and involution. There may be present at the same time small, new, tense vesicles; older, drying vesicopustules, and, in addition, dark-colored crusts which represent the remains of the first vesicles. This multiformity is one of the most distinguishing features of the eruption of chickenpox.

The *duration* of the individual lesions of chickenpox is brief. The vesicles, after reaching the acme of their development, become flaccid, and in from one to three days dry into crusts. The unruptured vesicle desiccates first at its central summit. Lesions which are ruptured by mechanical force give exit to a fluid which forms an irregularly shaped crust.

The fluid contained in the vesicle is at first as clear as water; it later becomes turbid and finally, if unruptured, quite purulent. During these changes the vesicle which has in the beginning a "dewdrop-like" appearance acquires a grayish or yellowish color.

True umbilication, such as is seen in the early smallpox vesicle, does not occur in chickenpox. There is sometimes seen a pinpoint-sized invagination of the surface of a vesicle due to the presence of a hair follicle. Commonly there is observed a central sinking in of some of the vesicles or vesicopustules due to partial evacuation and central drying. This is also seen in the late pustular stage of smallpox, and might be called a secondary umbilication.

As the vesicles of chickenpox begin to dry there not infrequently develops a flat, vesicular, spreading ring upon the border of the crust; beneath the raised-up epidermis is a little puriform fluid. The lesions may, as a result of this process, spread to the size of a silver quarter or half dollar. This condition is extremely common in smallpox and has been called "impetigo variolosa." The process being the same in chickenpox, the condition might be appropriately designated "impetigo varicellosa." The cause of these spreading sores is an infection of the varicellous sites with streptococci and staphylococci present upon the surface of the skin. In extensive eruptions where there is much of this impetigo, moderate elevation of temperature may develop, giving rise to a secondary fever.

The *extent* of the varicellous eruption is extremely variable. The total number of lesions in some cases may amount to but a half-dozen;

on the other hand, they may cover almost completely the entire cutaneous surface and number hundreds or even thousands. Thomas says, "as many as eight hundred have been counted or estimated." In a copious eruption in a young boy we counted one thousand four hundred lesions; shortly afterward in an older lad convalescent from scarlatina we encountered a much more extensive eruption. A photograph of this boy is shown in Plate XLII. We estimated that there were in the neighborhood of three thousand lesions upon the skin.

While neighboring and closely set vesicles may occasionally coalesce, one never sees a confluence of the lesions such as is observed in smallpox.

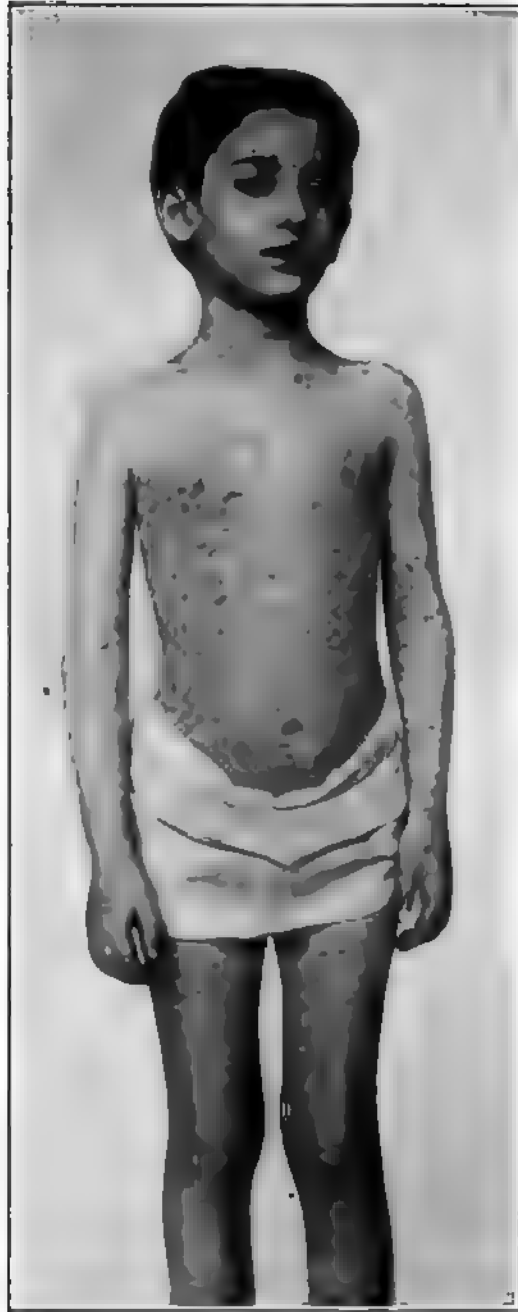
Scarring After Varicella.—It is not uncommon for some varicella lesions to be followed by scars. Indeed, it is rather the rule for patients to have one or several cicatrices which persist after the disappearance of the eruption. These are from pinhead to pea sized, rounded or oval, and excavated to a variable degree. In severe cases the number may reach a half-dozen or a dozen or more. They are never, however, as numerous as is seen in smallpox. The scars result from a destruction of the papillary layer of the true skin; this may be due to secondary infection as a result of scratching, but it may occur entirely apart from this cause. Chickenpox vesicles at times break down early and produce a necrosis of the underlying corium; the ulcer left heals with the formation of a depressed scar. Occasionally a hypertrophic scar or sort of keloid forms at the site of these losses of tissue.

The *mucous membranes* are not infrequently the seat of varicellous lesions. It is quite common to find a few vesicles upon the soft and hard palate, and these in doubtful cases are of diagnostic importance. Lesions are also occasionally noted upon the buccal mucous membrane, tongue, and posterior pharyngeal wall. Situated in these regions the flaccid roof of the vesicle soon ruptures, leaving at first a grayish pellicle of epithelial debris and later a circumscribed superficial abrasion, surrounded by a reddish areola and resembling to some extent the sore of aphthous stomatitis. The eruption in the mouth is usually scant, even in cases characterized by an abundant cutaneous outbreak. The exanthem, as a rule, appears synchronously with the eruption on the skin, but it may precede it. We know of a colleague who was perplexed by the appearance of a circumscribed patch on the posterior pharyngeal wall of his daughter, but who later discovered that it was an early varicellous lesion preceding the general eruption by about twelve hours.

Henoch has seen varicellous vesicles on the gums and also on the conjunctival mucous membrane. Thomas observed the latter attacked only when the contiguous portion of the eyelid was affected. He likewise under similar conditions noted involvement of the nasal mucous membrane.

Marfan and Halle have recorded two cases of involvement of the larynx, one necessitating tracheotomy. The other case succumbed to other complications and on autopsy the remains of a vesicle were found on the right vocal cord.

PLATE XLI.



An Unusually Extensive Eruption of Chickenpox in which the Lesions were Estimated to Reach 3000 in number.

PLATE XLII.



**Extensive Eruption of Chickenpox. Same patient
as Plate XLI.**



100

Varicellous lesions are occasionally found in the vestibule of the vagina and upon the prepuce, in which regions the accompanying swelling may cause difficulty in micturition.

As far as is known, chickenpox never attacks the mucous membrane of the stomach or intestines. Partridge, in 1887, presented to the New York Pathological Society specimens from a child that had died of varicella complicated by bronchopneumonia. In the large intestines were a number of excoriations which were regarded as chickenpox lesions.¹ This child had diarrhoea during life, and to our minds it is highly improbable that the intestinal lesions were of a varicellous nature.

Varicella in Adults.—We have preferred to consider chickenpox in the adult under special heading in order to give greater prominence to

FIG. 56



Chickenpox in an adult: second day.

the opinion that the frequency of this disease in adults has been underestimated. The assertions of many writers of prominence have caused varicella in adult life to be regarded as a *rara avis*. Thomas, whose teachings are based upon a large and well-digested experience, states: "Varicella is a disease of childhood, and attacks by preference young children, and even sucklings. In children over ten years of age attacks are infrequent, and *I never saw an adult suffering from varicella.*" And again, "the predisposition (to varicella) is wont to vanish of itself spontaneously about the eleventh year."² Von Jürgensen³ remarks: "With regard to the differences between variola and varicella, it is important to state that the latter is, if not wholly, yet practically limited to the age of childhood—the first ten years of life;" and, further on, "Varicella is a disease which is quite peculiar to the age of childhood."

¹ Quoted by Jennings. Keating's Cyclopaedia of Diseases of Children, p. 761.

² Thomas. Ziemssen's Cyclopaedia of Medicine. American edition, 1875, pp 8 and 27.

³ Nothnagel's System of Medicine. American edition, pp. 288-289.

Jonathan Hutchinson,¹ in a wide experience, saw one or two cases about the age of twenty and states that "a point of great interest in varicella is the almost complete immunity of adults."

Bohn encountered chickenpox but once in an adult, in a patient aged sixteen years, and J. Lewis Smith likewise saw but one case. Corlett² says: "During a period of twenty years in which the writer has been occupied in studying eruptive disorders, not a single instance has occurred in which varicella appeared after the fifteenth year."

The statements of these various observers would lead one to regard chickenpox in adult life as a great rarity. We grant that adult varicella is not an every-day occurrence, but that it is not of excessive rarity is evidenced by the fact that within eighteen months we have seen no less than 16 cases in the city of Philadelphia. During the past thirty-two years (1870 to 1902) there have been admitted into the Municipal Hospital 35 cases of adult varicella. Nearly all of these cases were sent into the hospital under the erroneous diagnosis of smallpox. We were enabled to successfully vaccinate all those who were not protected by previous vaccination.

In addition to these 35 cases we have seen 5 other cases within the past two years, (1901-02) the particulars of which we are able to recall.

TABLE OF AGES OF ADULT CASES OF VARICELLA.

Two were . . . 18 years old.	One was . . . 31 years old.
Three " . . . 19 " "	Three were . . . 32 " "
Five " . . . 20 " "	" " . . . 34 " "
Two " . . . 21 " "	Two were . . . 35 " "
" " . . . 21 " "	One was . . . 36 " "
Three " . . . 22 " "	Two were . . . 36 " "
One was . . . 23 " "	" " . . . 39 " "
Three were . . . 24 " "	One was . . . 40 " "
Four " . . . 25 " "	" " . . . 42 " "
One was . . . 26 " "	" " . . . 43 " "
Two were . . . 27 " "	" " . . . 48 " "
One was . . . 28 " "	
Four were . . . 30 " "	Total 51.

Of these patients 32 were males and 19 females; 22 were negroes and 29 were whites. We have also seen a number of cases of varicella between the ages of ten and eighteen years, but these have not been included in the above table.

The history of a patient admitted into the smallpox wards some few months ago is of interest. An unvaccinated man, aged thirty-one years, was sent into the hospital with the diagnosis of smallpox; he was found to be suffering from a curious papular and purpuric eruption of undetermined origin. He was immediately vaccinated on both arms and on the leg. The vaccinations were all successful, but at the end of ten days he fell ill and developed about a half-dozen variolous lesions. He was discharged from the hospital about ten days later. About a week afterward, he developed at home a fairly extensive eruption of

¹ Quoted by J. L. Smith. *Medical and Surgical Diseases of Childhood*, 1896, p. 229.

² *Infectious Exanthemata*, Philadelphia, 1901, p. 165.

chickenpox. It was evident that this had been contracted in the hospital from a man suffering from varicella who was sent in as a case of smallpox, and who was placed in a separate ward with the above-mentioned patient about a week before the latter's discharge. It is interesting to note that this patient successively passed through attacks of cowpox, smallpox (varioid), and chickenpox.

The underestimated frequency of chickenpox in adults is further attested by the figures which Wanklyn¹ presents of the cases of varicella sent to the diagnosing station of the Asylums Board of London during the smallpox epidemic of 1901-1902. Of 200 cases of chickenpox which were seen, 16.7 per cent., or 33 cases, were over eighteen years of age.

Lys² reports a family outbreak of chickenpox attacking three sisters, all adults. On the ground that chickenpox was rare in adult life, the two sisters were permitted to associate with the one originally attacked, with the result that they both contracted the disease.

There are certain features of adult varicella which deserve mention, inasmuch as they are not common in chickenpox in children.

It is not rare for adults to feel ill a couple of days before the appearance of the varicellous eruption. There may be malaise, chilliness, headache and some backache, nausea and moderate rise of temperature to 101° or 102° F. These symptoms are similar to those observed in smallpox, but are less severe. High fever, intense backache, repeated vomiting, and prostration are absent in chickenpox. Every now and then one will see cases of varicella in adults in which quite indurated papules will be observed on certain parts of the body. It is particularly on the thick skin of the forehead that these are seen. Typical varicellous vesicles, however, will be found elsewhere upon the cutaneous surface. A significant sign in many of these cases is the presence of vesicles here and there which have undergone rapid rupture and crusting, with the production of a blackish or bluish-black scab and depressed in the centre; the borders of these lesions are still vesicular. They present the appearance of having been excoriated by scratching.

COMPLICATIONS AND SEQUELÆ OF CHICKENPOX.

Varicella is one of the least dangerous of the various exanthematous diseases, both as regards mortality and liability to complications. Nevertheless, a sufficient number of rare complications has now been recorded to show that the affection is not entirely devoid of danger to life. Most of the complicating conditions result from infection of the skin at the site of the varicellous vesicles.

It is extremely common for the partially dried vesicle to spread upon the border in the form of flat pustules; or blebs of considerable size may be formed which dry into yellowish friable crusts. These spreading pustules may attain the diameter of a silver half-dollar. This peripheral

¹ *British Medical Journal*, July 5, 1902.

² *Lancet*, May 12, 1883.

extension is due to infection of the lesion with the pyogenic organisms commonly found upon the skin, and might appropriately be designated *impetigo varicellosa*. Most well-marked cases of chickenpox show some lesions which become the seat of impetigo. This secondary infection is not nearly as pronounced as is seen in smallpox; in severe cases of the latter disease, an extensive *impetigo variolosa* almost invariably occurs.

Trousseau¹ states that in an epidemic of chickenpox which prevailed in the Necker Hospital the fever ceased when the malady began, and during from fifteen to forty days *pemphigoid blebs* appeared on different parts of the body, leaving, on the surfaces which they had occupied, ulcerations exactly like those of pemphigus, which ulcerations continued for six weeks or two months.

The "sores" so frequently seen in chickenpox, particularly when the lesions are scratched, represent impetigo lesions. When these sores are numerous a moderate elevation of temperature (101° to 102° F.) may develop and persist for several days.

As a result of this same infection the neighboring glands may become enlarged and, in rare cases, undergo suppuration. *Boils* and *subcutaneous abscesses* may occur as a result of pyogenic infection. These are not infrequently seen upon the scalp, although any portion of the cutaneous surface may be attacked.

Erysipelas.—Erysipelas has been reported as occurring after chickenpox. Freyer² speaks of a case of erysipelas migrans complicating varicella, and Holt³ states that he has known of "three fatal cases of chickenpox resulting from erysipelas, beginning about the pocks." When we remember that erysipelas is a not uncommon complication in smallpox, it is not surprising that it should occasionally occur in varicella.

Pyæmia.—A remarkable case of pyæmia resulting from staphylococcic infection through the varicella lesions is reported by Brunner.⁴ The child had a suppurative inflammation around the elbow-joint, followed by a double parotitis and abscess of the left middle ear, ending fatally on the ninth day. Autopsy disclosed the presence of pus in the anterior mediastinum, the pericardium, the bronchi, the spleen, and the kidneys. The staphylococcus pyogenes was recovered from the blood, pus, and urine during life.

Lohr also records a death from chickenpox resulting from mixed infection with the staphylococcus pyogenes aureus.

Disseminated Gangrene.—Literature contains numerous references to a serious complication of chickenpox which was called by Hutchinson *varicella gangrenosa*. We have purposely avoided this name in the head line, inasmuch as this gangrenous condition is not to be regarded as a variety of varicella or even as a complication peculiar to this disease. It may occur also in vaccinia, variola, scarlatina, typhoid fever, and in

¹ Page 137.

² Deutsche med. Wochenschrift, 1878, iv. pp. 111-113.

³ Loc. cit.

⁴ Quoted by Brown. Article on "Varicella." Twentieth Century Practice of Medicine, 1898.

PLATE XLIII.



Impetigo Varicellosa. A pyogenic condition analogous to but milder than that which develops about variolous pocks.



various pustular dermatoses; it is true, however, that it most commonly complicates varicella.¹

In mild cases but one or several varicellous lesions may undergo necrosis; in more extensive cases many of the vesicles become involved. The vesicle may either become converted into a bleb, the gangrenous process beginning beneath this epidermal elevation, or the vesicle may dry into a dark crust and enlarge upon the periphery. Upon removal of the crust a sharply margined, punched-out, freely discharging ulcer is seen. A dusky-red areola surrounds the ulcer or eschar. In extensive cases the temperature rises to 104° or 105° F., and the patient rapidly sinks. Lung complications, particularly pulmonary infarction, are common. Mild cases of gangrene may recover. The affection is most common in debilitated infants, more especially those in whom the varicella is preceded by some other illness. In Griffith's case the chickenpox was preceded by measles, diphtheria, and pneumonia.

Cases of gangrenous varicella have been reported by Hutchinson, Demme, Abercrombie, Andrew, Crocker, Büchler, Jamieson, Löwenhardt, Payne, Stanifooth, Haward, Vierordt, Griffith, Lockwood, Silver, Woodward, and others.

We have, on several occasions, observed localized gangrene occurring at the site of smallpox pustules; these cases all terminated fatally. Stokes,² of Dublin, reports a case of vaccinia gangrænosa ending in recovery.

Synovitis and Arthritis.—Synovitis and arthritis have been reported as rare complications. Laudon³ and Perret⁴ have both published examples of joint involvement in chickenpox. The patient of the former, a boy aged four years, developed high fever early in the course of varicella, followed by marked swelling of the left elbow-joint. Recovery took place after several weeks.

Semtschenke, quoted by Rille, saw 2 cases of purulent pleurisy and purulent arthritis in an epidemic of chickenpox in Russia.

Högyes reports a case of varicella in a seven-year-old girl followed by nephritis and subsequently by an inflammation of several joints, accompanied by high fever and ending in recovery.

Braquehayé saw a purulent arthritis of the knee and elbow develop on the ninth day of a varicella which was apparently running a normal course. Despite incision and drainage death resulted. On autopsy a septic endocarditis was also discovered.⁵

Marfan and Halle⁶ describe 2 cases of serous *involvement of the larynx* through the presence of varicellous vesicles. In one case, in a boy of three years, tracheotomy was performed, the patient recovering. In the other, a child of nine months, with a well-marked chickenpox, developed

¹ An excellent description of this affection is given by Crocker under the title of "Dermatitis Gangrænosa Infantum." Text-book of Diseases of the Skin. American edition, 1903, p. 535.

² Dublin Journal of Medical Sciences, June, 1880.

³ Deutsche med. Wochenschrift, Leipzig, 1890, xvi. p. 567.

⁴ Province méd. Lyon, 1889, iii. pp. 256-261.

⁵ Quoted by Brown. Twentieth Century Practice of Medicine.

⁶ Quoted by Brown. Ibid.

stridor and dyspnoea; diphtheria bacilli were absent. Bronchopneumonia and diarrhoea supervened and death resulted; the post-mortem examination revealed the presence on the right vocal cord of a round, shallow ulcer, evidently the remains of a varicella vesicle.

Nephritis.—Nephritis is one of the most serious of the complications and sequelæ of varicella. While it occurs in only a very minute percentage of cases, there are in the literature a sufficient number of recorded instances to cause physicians to keep in mind the possibility of its development and to watch the kidneys in the treatment of this otherwise trivial disease.

Henoch¹ was one of the first to mention nephritis as a complication and reported 4 cases following chickenpox. Janssen,² Högyes,³ Oppenheim,⁴ Brunner,⁵ Unger,⁶ Rille,⁷ Schwab, von Jürgensen⁸ and Dillon Brown⁹ have all described similar cases.

The nephritis usually comes on during the first or second week of the disease. It varies in severity as does this complication in other infectious diseases. In severe cases an abundance of albumin and tube casts may be present in the urine. As a rule, the nephritis is mild, recovery taking place promptly. Dillon Brown, however, reports a case in which the kidney involvement after a mild attack of varicella ran a chronic course, ending fatally some ten years later. Högyes' case terminated fatally through complication with pneumonia, and Rille reports an uncomplicated nephritis ending in death and showing on autopsy parenchymatous changes in the kidneys.

Bronchitis and Bronchopneumonia.—Bronchitis and bronchopneumonia are mentioned as complications by Meigs and Pepper, and Rille reports a peculiar form of pleuropneumonia ending fatally on the nineteenth day after varicella.

Association of Chickenpox with Other Exanthematous Diseases.—It is not at all uncommon for varicella to develop during convalescence from other acute exanthematous diseases, such as measles, scarlet fever, smallpox, etc. On the other hand, these diseases may develop in patients suffering from varicella. It is rather rare for these eruptive diseases to be synchronously present in their acutest stages; usually the second disease appears as the first is beginning to decline.

Chickenpox has repeatedly broken out in the diphtheria and scarlet-fever wards of the Municipal Hospital. Under these circumstances the varicella would naturally appear not earlier than the end of the second week of the original disease. We have often seen varicella appear in scarlet-fever patients who were profusely desquamating. We have also observed these two diseases present at the same time with vaccinia.

¹ Berliner klin. Wochenschrift, No. 2, January, 1864.

² Nedre Tijdsch., 1864, B. xx. p. 223.

³ Orvosi hetil., Budapest, 1865, xxix. pp. 11-16.

⁴ Berliner klin. Wochenschrift, December 26, 1867.

⁵ Aerztl. Mitth. a-Baden, Karlsruhe, 1868, xlii. pp. 49-52.

⁶ Wien. med. Presse, 1868, xxix. pp. 1449-1451.

⁷ Wien. klin. Woch., 1869; Deutsche med. Woch., 1891.

⁸ Nothnagel's Encyclopedia of Medicine. Article on "Varicella."

⁹ Twentieth Century Practice of Medicine. Article on "Varicella."

Chickenpox may appear during convalescence from smallpox. The following outbreak of chickenpox among thirty-three children convalescent from smallpox is of interest:

In November, 1900, a child suffering from chickenpox was sent into the Municipal Hospital of Philadelphia, under the erroneous diagnosis of smallpox. The true character of the disease was recognized and the child vaccinated. This patient did not contract smallpox, but succeeded in transmitting varicella to a number of other children in the ward. These in turn infected new patients as they arrived, and in this manner varicella remained in the children's ward for a period of three months. In all, thirty-three children suffering from smallpox were attacked. It should be stated that a much larger number of children escaped infection. Whether this was due to temporary insusceptibility or to their having previously had chickenpox, it is impossible to say. The attacks were in the main mild and the accompanying eruption moderate in extent. Inasmuch as the patients were exposed during the eruptive period of smallpox, the chickenpox eruption did not appear until after the variolous lesions had become crusted or were disappearing. The earliest onset of varicella was in a girl, aged seven years, who developed chickenpox on the seventeenth day of the variolous outbreak. In this patient the firm, compact, crusted lesions of smallpox appeared in strange contrast with the recent dewdrop-like vesicles of chickenpox. The patient's temperature had not yet reached normal, but was hovering about 100° F. at the time of the appearance of the chickenpox eruption. It then rose to 102° F., subsiding rapidly to 100° F., and in a few days again rising to 103° F. owing to the development of an abscess. In this child the two diseases may be said to have existed simultaneously.

The chickenpox efflorescence appeared in most of the patients from the twentieth to the thirty-fifth days of their smallpox eruption. As the majority of these children entered the hospital on the third or fourth day of the variolous eruption, it is seen that many of the patients did not contract chickenpox for about a month after they were exposed. Inasmuch as the period of incubation of varicella is about fourteen to eighteen days, seldom longer than three weeks, this observation would suggest that during the early eruptive period of smallpox many of the children were not susceptible to the infection of chickenpox. To generalize, we should say that most of the little patients received the infection of varicella during the desiccative stage of smallpox or at about the end of two weeks of the smallpox eruption.

Smallpox and chickenpox may actually exist at the same time. Trousseau states that Delpech published a paper in 1845 in which he reported the simultaneous presence in a child of the eruptions of chickenpox and smallpox. We have seen one such case ourselves, the attendant circumstances of which leave no doubt as to the correctness of the diagnosis.

Coincident Smallpox and Chickenpox.—S. F., a girl aged five years, developed an eruptive disease which was regarded by a physician as suspicious; thereupon two other physicians independently visited the

patient and pronounced the disease to be chickenpox. The lesions dried up in the usual time, but two weeks later the girl became ill and developed typical smallpox. It is undesirable to publish the circumstances, but the fact is established that the variolous infection was carried to the child's home at one of the visits above referred to.

Thirteen days after the above patient was first seen, a smaller sister, aged two years, developed the eruption of chickenpox. Twenty-four hours later the characteristic lesions of smallpox appeared upon her. It is to be noted that this child was exposed to the smallpox infection at the same time as her sister. On admission to the hospital the little patient was covered with firm variolous papules. The face, arms, and legs were profusely involved, the trunk to a lesser extent. Upon the forehead near the border of the hair were two crusted and superficially ulcerated varicella lesions. A half-dozen or more varicellous lesions were also observed upon the back and a few on the abdomen and chest. Upon the lower portion of the back was a comparatively recent chickenpox vesicle just beginning to dry. The subsequent course of the case left no doubt as to the variolous nature of the second eruption. Two other children of this family who were protected against smallpox by previous vaccination showed crusted varicellous lesions upon different portions of the body.

THE PATHOLOGY OF CHICKENPOX.

The Skin.—Unna excised a characteristic "chickenpox" lesion from an eight-year-old boy on the second day of its existence. The following description is condensed from Unna's detailed findings:

In contrast with the central depression in the variolous vesicle the vesicle of varicella is tent-shaped, with the central point at the summit. The lateral walls rise obliquely from a broad base toward the roof, which is formed by a few stretched, horny scales. From these cellular partitions radiate downward as in smallpox. The chickenpox lesion is consequently divided like the smallpox lesion, but the point where the septa join lies not in the centre of the base, but in the covering or roof. The cavity proper only occupies the upper part of the much-widened prickle layer. It is limited beneath by the deeper strata of the prickle layer, which show pathological changes. In the centre the cavity extends downward to the papillæ of the corium, which are swollen and enlarged and which project into the cavity. The roof of the vesicle is formed by the original horny layer with the addition of a few layers of flattened transitional epithelium.

The degenerative changes in the cells of the rete mucosum are typically represented in varicella and can be better studied in this disease than in variola, for in the latter affection the onset of suppuration obscures the process. The early pus formation and the slowness of the process are the chief features which distinguish the cavity formation in smallpox from that in chickenpox. Extensive *fibrinoid metamorphosis* of the epithelium takes place as in variola. The varicellous process commences with the *reticulating liquefaction* of a few prickle cells of

the central and upper prickle-cell layer, in the middle of the first appearing congestive spot. The completely liquefied, confluent cavities rapidly dilate to form the vesicles; the persistent unliquefied epithelium is compressed to form the septa, as are the cells above to form the cover. While this septate cavity chiefly enlarges by swelling upward, the *ballooning* colliquation proceeds in all of the epithelial cells of the base, especially at the centre of the pock, then at the lateral margin, and in all of the healthy epithelial cells of the centre.

Many of the colliquated cells assume the form of peculiar giant cells. Even the septa which run through the vesicle are frequently surrounded by ballooned giant cells. At the base of the chickenpox lesion the balloons form a loosely connected covering which runs over the central papillary apices, often only in a single layer. The contents of the vesicle, at the height of its development, consist of finely granular or coagulated fibrin, enclosing a few fibrinously degenerated, compressed or ballooned epithelia and almost no wandering cells. The cutis shows a marked dilatation of the bloodvessels, a moderate serous saturation, and a considerable enlargement and multiplication of the cells about the vessels; the emigration of white corpuscles is reduced to a minimum.

Notwithstanding its appearance, the vesicle of chickenpox is not unilocular. The absence of resultant scarring is due to the superficial position of the pock, the non-occurrence of suppuration, and the early repair by young epithelial cells.

Blood.—Engel¹ examined the blood of a five-year-old child during the height of the pustular stage of chickenpox. He found a moderate leukocytosis with 67 per cent. of neutrophiles, subsiding to 47 per cent. in three days after the healing of the pustules.

On the first examination no eosinophiles were present, but upon the second, they had risen to 16 per cent.

THE DIAGNOSIS OF CHICKENPOX.

Smallpox.—Chickenpox may usually be distinguished from smallpox without much difficulty. In exceptional instances, however, the diagnosis may present perplexities which may cause even a physician experienced in these diseases to delay in pronouncing definitely as to the nature of the disease. Errors may occur through regarding a mild smallpox as chickenpox, or looking upon a severe varicella as variola. The points of differential importance are as follows:

1. **The Vaccinal Condition of the Patient.**—If a child under five or six years of age presents an eruption which exhibits features both of chickenpox and of smallpox, the presence of a typical vaccinal cicatrix would constitute strong presumptive evidence against the variolous nature of the exanthem, for successfully vaccinated children of this age do not acquire smallpox save under extraordinary circumstances.

¹ XV. Congr. für innere Med., 1897.

The same evidence would obtain in an adult successfully vaccinated within a similar period of time.

2. **Initial Symptoms.**—The appearance of the smallpox eruption is preceded by two or three days by an illness characterized in its most complete form by chills, fever, headache, backache, vertigo, nausea

FIG. 57



An unusually sparse smallpox eruption in an unvaccinated child. vesicles in a head position.

FIG. 58



Chickenpox eruption. vesicles easily broken, leaving abraded bases.

and vomiting, prostration, and general pains. The more severe the oncoming eruption, the more pronounced are these symptoms apt to be. The syndrome is often incomplete, the invasive illness presenting but a few of the above-mentioned symptoms. In exceptionally mild cases one may not be able at all to elicit a history of a prodromal stage. It is extremely uncommon, however, for this to occur, and the existence

of premonitory symptoms should always be regarded as a matter of great differential importance.

Except for occasional malaise a half-day or so before the appearance of the chickenpox eruption there is, in the vast majority of cases, no prodromal stage. We have recently had the opportunity in the Municipal Hospital of studying an outbreak of chickenpox among convalescents from scarlet fever. The continuous temperature records show that in nearly every case the eruption appeared before any pyrexial elevation occurred. Occasionally in adults, chickenpox may, however, be preceded by a prodromal illness suggestive of but milder than that observed in smallpox. These patients seldom experience vomiting or prostration, and the febrile elevation is, as a rule, moderate.

3. Constitutional Symptoms.—The fever and prostration in the eruptive stage are usually more severe in smallpox than in chickenpox. This is not an invariable guide, however, as severe cases of varicella are accompanied by higher temperature than very mild cases of smallpox.

4. Distribution of the Eruption.—It is a well-known and important fact that the smallpox eruption attacks with predilection the face and distal portions of the extremities. Upon the trunk, and especially the abdomen, the lesions are nearly always more sparse. In chickenpox the eruption is usually most profuse on the trunk, particularly the back, and relatively sparse on the wrists, hands, feet, and face. In general, it may be stated that smallpox prefers the exposed surfaces and chickenpox the covered.

It has been stated that chickenpox does not attack the palmar and plantar surfaces. This statement is erroneous, inasmuch as the palms of the hands and soles of the feet are every now and then attacked in pronounced cases. Of course, one never sees such a profusion of lesions in these regions as is observed in smallpox.

5. Extent of the Eruption.—The number of lesions upon the skin should not be regarded as important evidence. An unvaccinated child admitted some months ago into the Municipal Hospital had but five lesions upon the entire cutaneous surface. On the other hand, a lad with chickenpox occupying a different ward had about 1400 lesions and another boy over 3000.

6. Character of the Lesions.—In smallpox the eruption begins as firm papules, which slowly increase in size and develop into vesicles and pustules. Not all variolous papules are shotty, but they are more deeply seated and have a more infiltrated base than the chickenpox lesions. The variolous vesicles are often harder than the papules. They are moderately uniform in size, and are often, although by no means always, umbilicated. The vesicles are multilocular and difficult to rupture with the finger-nail.

Chickenpox lesions may begin as maculopapules, but within a few hours some become frankly vesicular. The epidermal roof is thin and easily broken, permitting the exit of a clear, watery serum. With the collapse of the vesicle the infiltration seems to disappear and a superficial excoriation is often left. The vesicle is often unilocular, but

little diagnostic value should be placed upon the comparative degree of evacuation of variolous and varicellous vesicles with a needle. Chickenpox lesions vary greatly in size, some being as small as a millet seed and others as large as a finger-nail. They do not become umbilicated save by central caving in or desiccation. The early drying, with the production of a depressed, blackish crust in the centre and irregular puckering of the vesicle or pustule on the periphery, is highly characteristic of chickenpox.

It is not rare in an extensive eruption of varicella to find one or several vesicles which resemble variolous vesicles, and, on the other hand, in smallpox to occasionally see a few superficial vesicles which resemble those of chickenpox.

7. Manner of Eruption.—The eruption of smallpox comes out without interruption in the course of twenty-four to forty-eight hours. The lesions show, therefore, a quite uniform development. (It should be remarked, however, that the eruption on the face is always a little in advance of the development elsewhere.) The chickenpox eruption comes out in crops on successive or alternate days, and the lesions may be seen in varying stages of development. The coexistence of recent tense vesicles, older puckered vesicopustules, and dried crusts is highly characteristic of the disease.

8. Course of the Eruption.—Smallpox lesions undergo a gradual evolution from papule to crust in the course of ten to twelve days (in modified cases five to six days). Chickenpox lesions last from two to four days and then crust. The crusts of smallpox are dense and compact, while those of chickenpox are thin and friable. The presence of numerous hard, mahogany-colored crusts embedded in the horny layer of the palms and soles bespeaks smallpox.

There is no one characteristic symptom on which a differential diagnosis between smallpox and chickenpox can be based. The case is to be viewed in all its aspects and a diagnosis made from the history and the associated local and constitutional manifestations. A due sense of proportion should be exercised in attributing proper weight to the presence and absence of the various symptoms. Even when this is done there are occasional cases in which twenty-four hours' delay and observation are desirable in order to definitely establish the diagnosis.

Impetigo Contagiosa.—If chickenpox is seen after the desiccation of the vesicles the disease may be confounded with impetigo. Indeed, impetigo is commonly engrafted upon a varicella, in which event the lesions spread upon the borders in the form of a vesicular ring. Impetigo contagiosa is characterized by the formation of vesicles or blebs which rapidly become pustular, rupture, and form superficial crusts. The face is the seat of predilection and is usually exclusively affected, although the hands, and in rare cases the trunk, may present lesions. The vesicles are thin-roofed and flaccid, seldom exhibiting the tenseness of varicella vesicles. The patient, as a rule, suffers no constitutional disturbance at all. The mucous membrane of the mouth is exempted. The lesions do not appear, as in varicella, in several crops, but increase

irregularly as a result of finger inoculation. The disease is caused by inoculation of the skin with certain pyogenic organisms.

Varicella runs a briefer course and the lesions disappear in a short time without local treatment; the existence of antecedent cases of chickenpox, or the development of later ones, after an interval of two weeks constitutes strong corroborative evidence.

THE PROGNOSIS AND TREATMENT OF CHICKENPOX.

Prognosis.—Chickenpox is, with the possible exception of rubella, the mildest of the acute exanthematous diseases. As Trousseau remarks, patients never die of varicella *per se*, although deaths in rare instances have occurred from complications. Most of the complications which have been recorded have been wound infections—impetigo, erysipelas, abscesses, gangrene, etc. With the exception of the first-named condition, these are extremely rare. Varicella may at times induce an anæmia or general failure of health which may predispose to tuberculosis.

Treatment.—When chickenpox appears in a household it is scarcely necessary to isolate the patient. Varicella is such a mild disease that it is just a question whether children in good health should not be allowed to take it. Those who reach adult life without passing through the disease are apt to contract it at times under awkward and embarrassing circumstances. When children are weakly or suffering from some other disease, they should, if possible, be protected against chickenpox. When isolation is carried out it should be continued until detachment of all of the primary crusts.

The constitutional symptoms of varicella are ordinarily so mild as to require no internal treatment. Where there is febrile disturbance children should be kept in bed and upon a bland diet.

The local treatment is of considerable importance. When the vesicles become distended with pus, particularly those on the face, they should be evacuated and cleansed with a weak antiseptic solution. The following ointment will be found useful in preventing secondary infection of the lesions:

℞ —Acidi carbolici	gr. x.
Hydrargyri chlorid. mit.	gr. xv.
Pulv. amyli,	
Pulv. zinci oxid.	ʒi ʒij.
Petrolati	ʒss.

As has already been stated, some chickenpox lesions are followed by indelible scars; these may be due to an early necrosis involving the papillary layer of the skin, in which event they cannot be prevented. In other cases the scars are due to a slow ulceration the result of pyogenic infection of the lesions. Scratching is liable to produce scars by infecting the skin. In young children the finger-nails should be closely trimmed to prevent traumatism from scratching; when scratching cannot be otherwise controlled the hands should be enclosed in muslin

bags attached firmly about the wrists. Doubtless the rare cases of varicella gangrænosa are due to infection of the skin. It is important to keep the hands and the entire body scrupulously clean.

To relieve the itching which is not infrequently present, the following lotion will be found efficacious:

R—Acidi carbolici	gr ixx. to ʒj.
Glycerini	ʒj.
Sptz. vini recti	fʒss.
Aquæ	q s. ad	fʒvj—M.

S.—Use locally.

In severe cases it is important to examine the urine to be sure that a nephritis be not present. If the latter complication arises it should be treated upon the usual principles governing the care of this condition.

CHAPTER VII.

SCARLET FEVER.

Synonyms.—Scarlatina: German, *Scharlach*; French, *la Scarlatine*; Italian, *Scarlattina*; Spanish, *escarlatina*; Latin, *febris rubra*.

Definition.—Scarlatina is an acute, specific, infectious disease, characterized by a sudden onset with high fever, headache, vomiting, and sore throat, followed on the second day by a generalized punctiform rash which later gives rise to desquamation.

There is a tendency to the development of cervical abscess, otitis media, and nephritis. One attack usually confers immunity for a life-time.

History.—The origin of scarlet fever is involved in obscurity; there are many suggestive descriptions in the writings of the later Greek and Roman physicians, but none are sufficiently complete and explicit to warrant the conclusion that they referred to scarlet fever.¹ Malfatti² regarded the terrible epidemic (the pest of Thucydides) that swept Athens in 429 B.C. as scarlatina, but it is evident from a study of the symptoms of this malady that there is no adequate reason for such a view; indeed, angina was the only symptom that this pest had in common with scarlatina.

Some writers have believed that certain passages in the works of Hippocrates referred to scarlatina, but inasmuch as no mention was made by this careful observer of the most conspicuous symptom of this disease, namely, the exanthem, it may be accepted that the references in question pertained to another malady (in all probability diphtheria). Rhazes³ stated that measles of vivid coloration was more dangerous than that which was but moderately red. Rhazes may have seen scarlatina, but it is useless conjecture to construe such sentences as the one just mentioned as references to scarlatina.

Gregory⁴ says that scarlet fever "probably invaded the world soon after measles and smallpox made their debut, for the Arabian physicians describe a species of measles which, from the extent of the desquamation, we may be assured was scarlatina."

Not until the sixteenth century is reached do we find convincing descriptions of scarlet fever. Ingrassias, of Palermo (1560), depicted this disease and was the first to properly differentiate it from measles.

He also called attention to the fact that the disease attacked an

¹ For much of the history herein contained we are indebted to the painstaking work of Noirot, *Histoire de la scarlatine*, Paris, 1847.

² Hufeland's *Journal der pract. Heilkunde*, Bd. xii., St. 3, p. 120.

³ *Cont. lib. xviii.*, cap. 8, f. 328, d. 383.

⁴ *Eruptive Fevers*, New York, 1851, p. 146.

individual but once, and that children were the most frequent subjects, but that adults were not invariably spared.

In 1574 Baillon described under the name of *rubiola* an epidemic malady which was prevailing in Paris; this disease he carefully differentiated from measles (*morbilli*).

Jean Coyttar,¹ of Poitiers, in 1578, described the features of an epidemic which differed both from smallpox and from measles, and which was strongly suggestive of scarlatina.

In 1610 an epidemic angina accompanied by a scarlet eruption is said to have raged in Spain, and to have passed thence to Naples, which was at that time under Spanish control. Ludovic Mercatus, in 1612, and Michael Heredia, in 1626, fully and clearly described these anginose cases. Sgambatus, an Italian physician wrote, in 1620, of "de pestilente faucium affectu neapoli saeviente," and his fellow-countryman, Oetius Clerus, described "de morbe strangulatorio" in 1636.

Daniel Sennert,² of Wittemberg, in the first half of the seventeenth century (about 1625), described the disease scarlet fever as we see it at the present day. The rash, the desquamation from the seventh to the ninth day, and joint pains are all carefully and faithfully depicted. This is, perhaps, the earliest reference in literature which may be credited as pointing unmistakably to scarlatina. Sennert's son-in-law, Doering, saw a similar epidemic in Poland; he called attention to the occurrence of delirium, anasarca, and rheumatoid pains.

We are indebted to Sydenham (born 1624 and died 1689) for the name scarlatina or scarlet fever, and for the crystallization of the medical comprehension of this morbid process. It is claimed by Corradi that the designation "mala da scarlatina" was employed in 1527 by Lancellotti, but Hirsh believes the term was not applied to the disease later described under the name of scarlet fever. Sydenham's experience was evidently limited to normal and mild forms of the disease; he did not encounter the severe anginose forms which were shortly afterward (in 1698) referred to by Morton. The latter writer, however, obscured the concept of the disease by asserting his belief that scarlatina was a confluent form of measles. This erroneous conception has from time to time been revived at different epochs of the nineteenth century.

Diemerbroeck, the Dutch physician, in 1640, wrote of a disease under the title of purpura, which he believed to be a variety of measles, but which, according to Gregory, was obviously scarlet fever.

In 1665 an epidemic of scarlatina occurring in Poland was described by Schultz under the name of purpura epidemica maligna; the title suggests that the disease prevailed in virulent form.³ Toward the end

¹ Thærei Alaniensis, cons. et méd. regis, "de febre purpura epidermale et contagiosa, libri duo," Parisiis, 1578.

² Opera Omnia, tome vi, lib. 5, cap. 12, p. 183.

³ Scarlatina was first observed in Hungary by Rayger; in Leipzig, by Ettmüller and Lange, in Modena, by Ramazzini, and in Augsburg, by Schroeck. It appeared in Scotland toward the end of the seventeenth century, for Sir Robert Sibbald, physician to the Court of Charles II., said, in 1694, that the disease had so recently appeared in the kingdom that he would not hazard an opinion upon it.

of the eighteenth century and in the early part of the nineteenth, scarlatina seemed to acquire an augmented malignancy. The increased frequency and severity of scarlatina in the beginning of the nineteenth century was speciously attributed by Grundmann, Funk, and others to the introduction of vaccination. Noirof pertinently remarks that vaccination has influenced the occurrence of scarlatina by delivering up to it and to other diseases of infancy multitudes of infants who without vaccination would have been destined to succumb to smallpox at an early age.

During the eighteenth century epidemics of scarlatina were observed in all parts of Europe.

A severe epidemic of scarlatina prevailed in London in 1747-48. This was described by Fothergill (then a young man entering the profession) under the title of "an account of the sore throat attended with ulcers, a disease which hath of late years appeared in this city, and in several parts of the nation." He had the clearness of vision to recognize that the disease was due to "the reception into the habit of a putrid virus or miasm, *sui generis* by contagion, and principally by means of the breath." The disease was for a long time referred to as Fothergill's sore throat.

The same epidemic extended to Plymouth, where, in 1751, it was carefully studied and reported by Huxham. In 1799 Withering published an account of an epidemic which was raging in Birmingham. He at first drew distinctions between the scarlatina anginosa of the older authors and Fothergill's sore throat, but later acknowledged that from an assiduous study of the disease for fifteen years he was convinced that they were one and the same disease.

In France an extensive epidemic occurred in 1750. The following French physicians of the eighteenth century left important writings on scarlatina: Navier Lorry, Dupuy de la Porcherie, Sauvage, and Desessarts. The disease was studied during this era in Germany by Storch and Plenciz; in Holland by de Haen, Keetell, and Bicker; in Italy by Parolini, Targioni, and Ghisi, and in Scotland by Brodly and Coventry.

Scarlatina first appeared in the United States, according to Thomas, in 1735. It is quite probable that the disease prevailed among the colonists from time to time in the pre-revolutionary period, although only after the American Revolution of 1776 did mention of scarlatina appear in medical literature. The first monograph on the subject published in this country was by Dr. Israel Allen; it was entitled *A Treatise on the Scarlatina Anginosa*, Leominster, Massachusetts, 1796.

According to Dr. Joseph M. Toner¹ scarlatina appeared in Boston in 1702 and again in 1735; in Kingston, Mass., in 1735; in Philadelphia in 1746, and in Connecticut in 1751. The disease became pandemic in 1790 and again in 1830. Scarlatina first made its appearance in Iceland in 1827, and in Greenland in 1847.

¹ Quoted by Thomas C. Minor, in a report to the American Public Health Association, 1875.

ETIOLOGY.

Despite the fact that the causative agent of scarlet fever has not yet been discovered, the statement may be made that the disease is produced by a specific micro-organism. Scarlet fever is so similar in its behavior and manner of transmission to other infectious diseases of proven parasitic origin that, reasoning by analogy, we are irresistibly forced to this conclusion. Not many years ago it was maintained by writers that cases of scarlet fever could arise *de novo*, independently of pre-existing cases. The spontaneous origin of infectious diseases is no longer credited by medical scientists of the present day. The channels of infection are often so devious and the manner of transmission so mysterious as to make the origin of these diseases in individual instances quite incomprehensible. But the mystery of an infection is dispelled and becomes as clear as the trick of the magician when the solution is at hand. The proposition may, therefore, be accepted that every case of scarlet fever has its origin in an antecedent attack in another individual.

Modes of Transmission of the Scarlatina Contagium.—The germ of scarlet fever is chiefly if not exclusively conveyed in two ways: (1) directly from a scarlatina patient to the newly infected subject, and (2) through the intermediation of infected objects.

The vast majority of cases of scarlatina doubtless result from exposure to persons suffering from the disease; this is freely admitted. A certain school of German writers, led by von Kerchensteiner, maintains that the disease cannot be conveyed by a third person. The clinical experience of numerous careful observers is strongly opposed to such an opinion. Indeed, there are recorded instances of such transmission which appear quite conclusive.

Dr. Loeb, of Worms, mentions the case of his three-year-old daughter who developed scarlet fever at a time when there were no known cases in the city. The origin of the infection was a mystery until it was discovered that a medical friend and colleague who had been at the house, and upon whose lap the little girl had sat for a long time, had some hours previously visited three cases of severe scarlatina in another city and had not changed his clothes. The disease manifested itself at the end of two days. The circumstances surrounding the case would seem to point in the strongest manner possible to the conveyance of the germs in the clothes of the physician.

Thomas saw a case "in which a nurse coming directly from a scarlatinous patient communicated the disease in the short space of three hours to a child who had almost recovered from a tracheotomy." He also quotes Zengerle to the effect that a healthy woman, after a visit to a scarlatinous patient, transmitted the disease to her daughter, who was the first patient affected in the whole city. Murchison was convinced, from the testimony he had received from numerous physicians, that the scarlet-fever infection was not rarely carried by them.

The infection commonly clings to objects which have come in contact with the scarlet-fever patient, such as bedding, clothing, books, letters,

toys, etc. Numerous instances are recorded in which such articles have transmitted the infection. Both Richardson and Peterson traced cases of scarlet fever to infection transmitted in letters. It is an important matter in infectious-disease hospitals that all outgoing mail be thoroughly disinfected.

The scarlet-fever contagium may *cling tenaciously and for a long time* to the sick-room and to certain objects contained therein. Murchison, on the testimony of Richardson, mentions an extremely sad illustration of this. A child having been seized with a fatal attack of scarlet fever in a country house, the three remaining children were quickly removed. After a lapse of several weeks one child that was brought home contracted in twenty-four hours an attack of scarlet fever to which he rapidly succumbed. The house was then thoroughly cleaned and the walls whitewashed, but the infection was not removed, for a third child that returned after four months took the disease and died in the same manner as the others. It is believed that the infection was retained in a thick layer of straw covering on the children's beds.

Von Hildebrand claims to have contracted the disease from a black coat which he had worn a year and a half before while attending a case of scarlet fever in Vienna.

The most remarkable claim of longevity of the scarlet-fever infection is mentioned by Boeck (quoted by Johannessen, *loc. cit.*), who relates the circumstance as follows:

"The children of a colleague of mine had obtained permission to play with some things in an old writing desk. In a drawer lay some hair that had been cut from two children that had died of scarlet fever *twenty years before*; since that time the drawer had not been touched. Now it was opened and the children took scarlatina. These cases were the first in the city, so that the probability is evident that the infection was transmitted in this way."

Immunity and Susceptibility.—There is no such universal susceptibility of persons to scarlet fever as is known to exist toward measles and smallpox. Experience teaches that but few people enjoy a natural immunity against these latter diseases. Many persons, however, escape contracting scarlet fever even though freely exposed to its infection.

The contagion of scarlet fever is a most *capricious* one; it may repeatedly spare an exposed individual and lead him to believe that he is immune against it, only to smite him at some subsequent period.

This *temporary immunity* against scarlet fever has been repeatedly noted by various observers. Nurses have frequently been observed during the closest attendance upon patients suffering from scarlet fever to remain free from infection, and yet later contract the disease. Such a case has recently come under our observation:

Mrs. X., aged thirty years, a private trained nurse, was brought into the Municipal Hospital on January 9, 1903, suffering from a well-pronounced attack of scarlet fever. She had never had the disease in childhood. During the past few years she estimated that she had nursed about fifteen cases of the disease. On November 17, 1902, she com-

pleted her service in connection with a severe case of scarlet fever in the suburbs of Philadelphia. A little over six weeks later she began to nurse a patient with puerperal scarlet fever. After being on duty four days she herself was taken with a scarlatina of average severity, which ran a typical course and was followed by profuse desquamation.

We recall the case of an ambulance driver at the Municipal Hospital who came in almost daily contact with cases of scarlet fever, and who finally at the end of several years contracted a well pronounced attack of the disease.

On another occasion one of the nurses at the Municipal Hospital contracted a well marked attack of scarlatina on returning to duty in the scarlet-fever wards after a year's absence. Prior to her departure she had nursed mixed cases of diphtheria and scarlatina for a period of three months.

It would appear in these cases that for some reason or other the resisting power of the subject is lowered at the time of infection; this explanation seems to us to be more plausible than the assumption that the attack is determined by an unusually intense infective agent.

In some instances it would appear that the temporary immunity against scarlet fever is overcome by infection through unusual channels. The puerperal state and surgical operations are said to favor the development of the disease.

Von Leube¹ gives an interesting account of an attack of scarlatina in his own person following a wound received in making an autopsy upon a patient who had died of an unusually severe case of scarlet fever. He states that he had considered himself perfectly immune, having been exposed as a child, and having attended any number of cases under all sorts of circumstances. Ten days after the post-mortem wound upon his finger he developed sore throat, and on the following day he vomited, had a "decided fever," and the scarlatina rash. The course of the disease was one of medium severity.

The susceptibility to scarlatina *commonly disappears in adult life*; at any rate, many adults who have never had the disease escape infection, although freely exposed. Patients suffering from scarlet fever have on numerous occasions been placed in the wards of general hospitals without appearing to disseminate the disease among other occupants of the ward. Such experiences illustrate the very limited susceptibility of persons who have passed the age of puberty.

During the past few years the students of the various medical colleges in Philadelphia have been conducted through the wards of the Municipal Hospital in order to study the various infectious diseases therein treated. About 700 students in all have taken advantage of this bedside instruction. They were taken into the scarlet-fever wards in which there were 100 or more cases of this disease, and remained from one to two hours in this intensely infected atmosphere. *About one-half of these students, according to their statements, had never had scarlet fever, and yet not a*

¹ *Specielle Diagnose der inneren Krankheiten*, Bd. II. p. 364. Leipzig, 1898.

single one contracted the disease. This is strong proof of the frequent abrogation of the susceptibility of adults to scarlet fever.

Epidemics Among Adults.—Vogl,¹ of the General Medical Staff of Bavaria, reports two epidemics of scarlet fever among the Bavarian troops at Munich. In 1884–85, during a garrison epidemic covering a period of 178 days, 125 out of 7442 soldiers, or 1.67 per cent., contracted the disease. The mortality rate was 4 per cent. In 1894–95, during a similar epidemic lasting 155 days, 311 out of 9608 troops, or 3.23 per cent., took scarlatina, of whom 1.2 per cent. died. The attack rate among exposed adults is thus seen to be very small.

Murchison estimated that the number of persons attacked with scarlet fever in England and Wales was considerably less than one-half of the number of births. It is evident, therefore, that the lessened susceptibility to scarlatina exhibited in adult life is not entirely due to protection granted by an attack in childhood.

This is also shown by the figures of scarlatina in virgin countries. From 1873 to 1875 an extensive epidemic² of scarlatina raged in the Faroe Islands. The disease had not been known in this locality for fifty-seven years and possibly had never occurred at all. From the carefully collected data of Hoff concerning the town of Thorshavn, the chief city of the islands, it is seen that of a population of 930 persons, 237 contracted the disease. Among the entire inhabitants of the islands, of whom none had ever had scarlatina, but 38.3 per cent. contracted the disease during this protracted epidemic.

Age.—Age is a most pronounced factor in the determination of susceptibility to scarlet fever. It is a general experience that infants under one year of age exhibit a lessened disposition to contract the disease; this is still more true of nurselings under six months, and in infants under three months of age scarlatina is excessively rare. The infrequency of the disease at this tender age may be judged by the statements of experienced observers in reference thereto.

Fleischmann³ saw no cases under six months of age; Eulenberg, none under eight; Thomas, none under five; Böning saw no cases under one year; Senfft saw but one patient under one year, and Gaupp only two. Haller observed a case at five months; Voit, one at two and a half months; Küpfer, one at two months; and Veit, one at two weeks.

This represents an extremely scant number when the large number of cases of scarlatina observed by these men is taken into consideration. In Johannesen's statistics of scarlet-fever deaths in Norway from 1862 to 1878, the number of infantile attacks is considerably greater. He reports 15 deaths from scarlatina under six months, and 93 under one year. In our own experience at the Municipal Hospital we have found that among 5000 cases of scarlet fever admitted into the hospital, about 1 per cent. consisted of infants under one year of age. We have on a number of occasions had infants a few months old brought into the

¹ *Münchener med. Woch.*, 1895, p. 949.

² Mentioned by von Jurgensen in Nothnagel's *Encyclopedia of Practical Medicine*.

³ Mentioned by Thomas in Ziemssen's *Encyclopedia of Practice of Medicine*, p. 180.

hospital with mothers suffering from scarlatina, but we have seldom observed them to contract the disease. We have seen them suckle at breasts covered with the scarlatinal rash, draw a febrile milk, and yet remain perfectly well.

The question whether there is a *congenital scarlatina* is most difficult to answer. Children are so commonly ushered into the world with a red rash that but little reliance can be placed upon the existence of an exanthem. Furthermore, it is not uncommon for the tender epidermis of the infant to peel off after some days and thus cause a desquamation. Baillou, Ferrario, Stiebel, Hüter, and others saw infants that were alleged to have scarlatina at birth (most of them being born of mothers suffering from scarlet fever at the time), but the facts do not appear to us to warrant the unreserved acceptance of the diagnosis. Murchison saw two pregnant women with scarlet fever, and in each case the child born at the time was free of the disease. Elsässer also saw a healthy babe born of a mother with scarlatina.

Children from two to five years of age appear to be most susceptible to the contagium of scarlatina. From five to ten years the attack rate is somewhat less, and after the period of puberty is reached the susceptibility to the disease is greatly lessened. No age, however, appears to guarantee absolute immunity against scarlatina inasmuch as persons even over the age of ninety-five have been known to contract the disease.

Murchison's valuable statistics of scarlet-fever deaths in England and Wales, covering the enormous number of 148,829, will give a fairly accurate idea of the incidence of the disease in the different age periods:

Under 1 year	9,999	or 6.7 per ct.
From 1 to 2 years	20,975	" 14.1 "
" 2 " 3 "	23,842	" 16.0 "
" 3 " 4 "	22,528	" 15.1 "
" 4 " 5 "	17,726	" 11.9 "
" 5 " 10 "	38,591	" 25.9 "
" 10 " 15 "	6,676	" 5.5 "
Total under 5 years	95,070	or 63.8 per ct.
From 5 to 15 years	47,267	
" 15 " 25 "	3,371	
" 25 " 35 "	1,806	
" 35 " 45 "	671	
" 45 " 55 "	331	
" 55 " 65 "	185	
" 65 " 75 "	88	
" 75 " 85 "	20	
" 85 " 95 "	4	
Over 95	6	
Total	148,829	

It will be seen from the above tables that considerably over one-half of the deaths of scarlatina occurred in children under five years of age. Almost 90 per cent. occurred in those under ten years, and over 95 per cent. under fifteen years of age.

These figures correspond very closely with statistics of scarlet-fever deaths in Berlin from 1875 to 1891, and with Johannesen's statistics for

Norway. As showing the fatal cases in children under one year, the latter statistics are of particular interest:

FATAL CASES OF SCARLATINA IN CHRISTIANA UNDER ONE YEAR OF AGE.
(JOHANNESSEN.)

1st month	0
2d to 3d month	3
4th " 6th "	12
7th " 12th "	78

The above deaths were out of a total of 1040 fatal cases.

Family Predisposition.—Some families, at times, exhibit an unusual susceptibility to scarlatina; this is manifested not only by several members of the family contracting the disease, but likewise by the severity of the attack. Thomas¹ recognizes "an intense family predisposition, showing itself by numerous and severe attacks in the family as soon as one infection has taken place in it." Trousseau says: "Scarlatina epidemics may be full of danger for an entire population, or they may assume this character only for a single family. The malignancy limits itself in a measure to a single hearth, and in such cases the disease is malignant for all persons that live within its circle." Henoch² expresses much the same idea; he says: "Striking to me appeared the fact that if scarlatina breaks out in a family, very frequently also a second and third child are taken off under similar conditions, and in this way whole families can die out."

Copeman,³ during a severe epidemic of scarlet fever in 1844, saw four children in a family die so suddenly that poisoning was suspected; a fifth child went through an ordinary attack of scarlet fever.

A somewhat similar instance has recently come under our observation. In the winter of 1902 we saw a family in which four children were smitten with scarlet fever. All fell suddenly ill with vomiting, which was attributed by the mother to free indulgence in candy. Soon the scarlatinal rash manifested itself. The eldest daughter, a girl of seventeen, died in five days; a second one had a temperature of 105° F., with intense prostration, and recovered, as did a third child, only after a most desperate illness. The infection in these cases was most virulent, and yet the prevailing type of scarlatina in the city at that time was quite mild.

These severe family epidemics are difficult to account for. Henoch presupposes a mixed infection in such cases. Thomas does not seek an explanation in an unusually intense infection, for he says "the infecting cases are frequently of a mild character."

Epidemics of this character are happily uncommon. In some instances there is a tendency to family immunity, the members thereof exhibiting an almost complete insusceptibility to the disease.

Climate.—According to Minor,⁴ who has in a most painstaking manner studied the prevalence of scarlatina in the United States, climatic conditions influence the spread of the disease. He says:

¹ Loc. cit., p. 175.

² Vorlesungen über Kinderkrankheiten, p. 654, third edition.

³ Jahresbericht, etc., der Gesamten Medicin. R. Virchow and Aug. Hirsch, vi. Jahrgang, 1871, vol. II. p. 247.

⁴ Loc. cit., p. 13.

1. "The zone of comparative immunity in the Eastern Hemisphere extends from 10° south latitude to 20° north latitude." (In this zone are found Sumatra, Borneo, India, and most of Africa.)

2. "A zone of comparative immunity in the Western Hemisphere extends from the equator to 10° north latitude." (In this zone are found Venezuela and the States of Colombia.)

3. "Another zone of comparative immunity in the Western Hemisphere extends from 30° to 35° north latitude." (In this zone are found South Carolina, Georgia, Alabama, Mississippi, Louisiana, Texas, and the northern part of Florida.) According to the vital statistics of the United States for the year 1900 these States, with the exception of Texas, had a remarkably small scarlatina mortality compared with other sections of the country.

4. "In times of pandemics, occasional epidemics occur at points within the zones of comparative immunity." The disease in these regions, however, attacks by preference the Caucasian race.

Minor furthermore says that in these countries, "lying for the most part in the tropics and near the equator, exposed to the direct rays of the sun, a *high mean annual temperature* is of course noticeable." This author, after discussing the climatic influences, concludes that "a very high temperature, combined with periodical humid atmosphere, is unfavorable to the development of any scarlatinous tendency."

Season.—Hirsch has studied the seasonal incidence of 435 epidemics of scarlet fever occurring in Norway, Sweden, Russia, Germany, Holland, France, Italy, Spain, and North America. Most of the epidemics occurred in autumn, as will be seen from the following figures: autumn, 29.5 per cent.; winter, 24.7 per cent.; summer, 24 per cent., and spring, 21.8 per cent.

In England, since the days of Sydenham, it has been recognized that scarlatina prevails most in the fall; 55,956 deaths in London from scarlatina during a period of twenty-four years gave the following percentages: autumn, 35.54 per cent.; winter, 23.85 per cent.; summer, 22.75 per cent.; spring, 17.87 per cent.

In the *United States* scarlatina is most prevalent during the *latter part of winter* and during the *early spring* months. The vital statistics for 1870 show the largest number of deaths in March. The first five months of the year exhibit a considerably greater mortality than the rest of the year:

SCARLATINA DEATHS BY MONTHS IN THE UNITED STATES IN 1870.

January	2205	September	927
February	2893	October	1090
March	2726	November	1281
April	2294	December	1705
May	2146	Unknown	5
June	1826		
July	1216		
August	1096	Total	20,830

Arranged according to seasons, the figures read as follows:

Spring	7166	Autumn	3208
Summer	3638	Winter	6303

The vital statistics of the United States for the year 1900, although somewhat differently presented with reference to scarlet-fever mortality, give similar results:

SCARLATINA DEATHS BY MONTHS PER 1000 OF DEATHS FROM ALL CAUSES
IN THE UNITED STATES IN 1900.

January	118.3	August	50.3
February	112.8	September	52.5
March	106.8	October	69.4
April	105.7	November	84.8
May	98.4	December	98.7
June	56.0		
July	46.3	Total actual deaths .	6333

Here again it is seen that the greatest mortality from scarlet fever is in the late winter and early spring months.

According to Murchison, epidemics of scarlet fever in France occur more frequently in the spring and summer months.

Johannesen classifies as follows 65,785 cases of scarlet fever occurring in Sweden from 1867 to 1878:

January	11.3 per ct.	July	6.6 per ct.
February	9.2 "	August	6.3 "
March	9.1 "	September	5.7 "
April	7.8 "	October	8.0 "
May	7.8 "	November	10.4 "
June	6.9 "	December	10.7 "

It is seen that the greatest number of cases occurred in November, December, and January.

In Berlin, from 1877 to 1883, there were 5428 deaths from scarlatina, with the following monthly mortality:

January	6.7 per ct.	July	8.0 per ct.
February	5.3 "	August	8.5 "
March	5.8 "	September	10.7 "
April	6.1 "	October	13.8 "
May	7.0 "	November	10.9 "
June	8.1 "	December	8.5 "

The greatest number of deaths occurred in autumn—September, October, and November, the maximum being reached in October.

From the various statistics presented it is seen that season apparently has some influence on scarlatina prevalence. The same months in different countries show, however, widely divergent figures.

The different character of the climate in the countries mentioned may account for the discrepancies in the monthly morbidity incidence. It will be necessary to carefully compare the climatic and meteorological conditions by month in the various countries before anything can be definitely said as to the influence of season upon the spread of scarlatina.

Minor¹ studied the influence of temperature on the prevalence of

¹ Loc. cit., p. 51.

scarlatina and came to the conclusion that the colder weather seemed to favor the scarlatinous tendency. He states that:

1. The scarlatinous tendency is but slightly, if at all, modified by a temperature ranging from zero to 65° F.

2. The scarlatinous tendency is decidedly modified and lessened by a temperature ranging from 75° to 80° F.

3. The scarlatinous tendency is almost entirely destroyed where there is a prolonged high temperature ranging from 80° to 85° F.

Influence of Urban and Rural Localities.—As would be naturally expected, the prevalence of scarlatina is greater in city than in country districts. This is to be accounted for by the more extensive intercourse between cities and by the greater crowding and more intimate contact of the people. The vital statistics of the United States for the year 1900 show a very distinct difference between the city and rural death rate by months:

DEATH RATE FROM SCARLATINA BY MONTHS IN CITIES AND RURAL DISTRICTS, PER 1000 OF ALL DEATHS.

	Cities.	Rural.
January	1.6	0.8
February	1.8	0.9
March	1.5	0.9
April	1.4	0.8
May	1.4	0.7
June	1.0	0.4
July	0.6	0.3
August	0.5	0.3
September	0.4	0.3
October	0.3	0.4
November	0.8	0.5
December	1.2	0.8

Scarlet fever is practically endemic in the great centres of civilization; the disease in the large cities of the world increases and decreases from time to time, but never dies out completely.

Altitude.—Minor¹ says in regard to altitude that "scarlatina prevails at all altitudes, epidemics occurring at New York, Providence, and Boston, on the Atlantic coast; at Pittsburg, Cincinnati, Chicago, Detroit, and St. Louis, in the interior of the continent; finally, among the mountains of Nevada, and at San Francisco on the Pacific slope. In order to determine whether altitude seems to modify or lessen the tendency to scarlatina, we shall group the States as follows: First group, States having average altitudes ranging from 150 to 600 feet, are Tennessee, Vermont, Kentucky, Georgia, North Carolina, Texas, Massachusetts, Maine, Maryland, Alabama, South Carolina, Arkansas, Connecticut, Mississippi, New Jersey, Rhode Island, Delaware, Louisiana, and Florida. Total population of this group, in 1870, was 14,597,384. Second group, States having average altitudes ranging from 600 to 1000 feet: Iowa, Wisconsin, Missouri, Michigan, New York, Pennsylvania, Ohio, Virginia, Indiana, Illinois, and New Hampshire. Total population

¹ Loc. cit., p. 54.

of this group, in 1870, was 21,506,599. Third group, States having average altitudes ranging from 1000 to 5400 feet: Nevada, California, Oregon, Nebraska, Kansas, Minnesota, and West Virginia. Total population of this group, in 1870, was 2,133,316. In these three groups of States, 20,159 deaths from scarlatina occurred—*i. e.*, 3333 in the first, 15,351 in the second, and 1475 in the third. If we analyze these figures, the following is the result:

Altitude.				Deaths.			
150	to	600 feet.	.	1 death to every 4380 of population.			
600	"	1000 "	.	1 "	"	1401 "	"
1000	"	5400 "	.	1 "	"	1447 "	"

“ Now, taking into consideration the density of population in the second group as compared with the third, together with the fact that scarlatina, being a contagious disease, should be more prevalent where it has the largest and densest population to prey upon, we conclude that altitude rather favors an increase of the scarlatinous tendency.”

A striking difference in the prevalence of scarlatina in certain of the European capitals has been observed. In London,¹ from 1868 to 1872, there were nearly 115,000 cases of scarlet fever. In Berlin, from 1877 to 1883, scarlatina caused 5428 deaths. On the other hand, during a period of five years in Paris, the total deaths from scarlet fever were only 67.

It is quite inexplicable why London and Berlin should suffer so severely from this disease while Paris possesses a comparative immunity.

Race.—There is strong evidence that *negroes* are *less susceptible* to scarlet fever than the whites, and, furthermore, that the mortality rate among the former is *very considerably lower* than in the Caucasian race. Minor,² writing in 1875, says: “The total number of blacks dying of scarlet fever in the Southern States was 107 out of a total black population of 3,713,327; so that 1 out of every 34,704 of the aggregate black population died of scarlatina. The total number of whites dying of scarlet fever was 446 out of a total white population of 4,811,962; so that 1 out of every 10,790 of aggregate white population died of scarlet fever. It will be at once noticed that the disease is much more frequent among the whites than among the colored population. During epidemics the whites have seemed to be the sufferers, and there is reason to believe that there is a certain immunity from epidemic scarlatina existing among the negroes of the South.”

During the Civil War³ 378 whites took scarlet fever, of whom 70 died, and 118 negroes contracted the disease, of whom but 2 died. Comparing the number of the white and black troops it is seen that the attack rate was 54 in the black race to 26 in the white; on the other hand 70 deaths occurred among the whites and only 2 among the negro soldiers.

The United States census of 1870 demonstrated the fact that the

¹ Mentioned by Forchheimer. Article in Twentieth Century Practice of Medicine.
² Loc. cit. ³ Medical and Surgical History of the Rebellion, vol. III., part I.

foreign-born population of the country was 5,567,229, and that 1 out of every 6105 died of scarlet fever. The population of the native-born whites was 28,120,788, of whom 1 out of every 1473 died of scarlet fever. The negro population was 4,880,009, of whom 1 out of every 16,886 died of the disease.

It is thus seen that scarlet fever destroyed, relative to the population, over ten times more whites than negroes. The census statistics of 1850 give somewhat similar results.

The United States census report of 1890 shows a scarlatina death rate among the whites of 14.2 per 1000 deaths from all causes to 2.7 among negroes. The figures of the 1900 census are almost identical—12.0 death rate among the whites as compared with 2.6 among the blacks. These statistics would indicate that the Caucasian race in the United States is six times more susceptible to scarlatina than the negroes.

Inoculability of Scarlatinal Virus.—Attempts, doubtless based upon the success achieved by inoculation of smallpox, have been made to induce a mild form of scarlet fever by this process. These experiments, though often contradictory, have thrown some light upon the etiology of scarlet fever.

In 1834 Miquel reported to the French Academy that he had inoculated a number of children with the fluid of scarlatina vesicles. The rash was localized to the region of inoculation. Miquel alleges that complete immunity against scarlet fever was conferred. The reported facts made it very doubtful that scarlatina was actually transmitted. In two cases inoculated by Rostan the rash appeared seven days after inoculation. According to the statement of Guersant,¹ Petit-Radel made unsuccessful attempts to produce scarlatina by the introduction of epidermal scales beneath the skin of previously unattacked persons.

On the other hand, Stoll is reported to have produced the disease by rubbing into the skin scales from a case of scarlet fever. These experiments are seen to be contradictory and permit no conclusions to be drawn.

A much more convincing case is the accidental inoculation of Dr. Rupprecht² with mucus from the trachea. This physician had performed a tracheotomy on a mixed case of scarlatina and diphtheria. In insufflating the lungs through an elastic catheter, he received some mucus into the mouth. Sixty hours later an angina developed and in seventy-eight hours a chill. The eruption was irregular, but the diagnosis was said to be certain.

Recently some rather conclusive inoculation experiments were carried out by Stickler³ in an effort to induce a mild attack of scarlet fever. Mucus from the mouth and throat of scarlatinal patients was mixed with a 1:600 solution of carbolic acid and injected subcutaneously into ten children. Scarlet fever occurred in each child. The period of incubation varied between twelve and seventy-two hours, and averaged thirty-two hours. The author found that the attacks were too severe to

¹ Quoted by Thomas. *Loc. cit.*

² Ein Fall von Scharlach. *Wiener med. Woch.*, 1862. *Hauptblatt*, p. 435.

³ *Medical Record*, September 9, 1899.

warrant further inoculations, and, therefore, desisted. Incidentally the fact was proven that the mucus of the upper air passages contains the *causa causans* of the disease.

From the experiments quoted we are not justified in drawing any conclusions as to the presence in the skin of the infectious principle. A possibility of error, always to be kept in mind, is that persons inoculated with scarlatinal virus may have contracted the disease through exposure in the ordinary manner.

Mode of Reception of the Scarlatinal Infection.—The scarlatinal poison is ordinarily received into the system through the upper air passages. It would seem that the genital tract in puerperal women and cutaneous wounds may also offer a point of ingress for the infection. But in the vast majority of cases the poison is “breathed in” just as in the other acute eruptive fevers. Whether the virus effects its entrance into the blood in the lungs, or at some point along the respiratory avenue, is a difficult question to answer. Dowson, in 1893, endeavored to prove that the first and essential localization of the scarlatinal poison was in the throat. Bergé,¹ following this view, maintains that scarlatina is primarily a local tonsillar infection, and that the eruption both upon the cutaneous and mucous surfaces is the result of the action of an erythemogenic toxin generated in the tonsils. The streptococcus in one of its virulent forms is regarded as the causative agent of the disease. The view is advanced that the infection may exceptionally gain entrance into the system through other channels, as in the case of surgical and puerperal scarlatina. The author cites a number of cases to show that in puerperal and surgical scarlatina the primary tonsillitis is absent, although the buccopharyngeal enanthem may be present.

The theory and facts presented by Bergé are of interest, but until the cause of scarlatina is satisfactorily demonstrated, we will doubtless remain in ignorance of the site of invasion of the scarlatinal virus.

Period of Infectivity of Scarlatina.—In discussing this subject we wish to draw a distinction between the duration of infectiousness of the scarlatinal virus within and without the patient. Reference has already been made to the longevity of the virus outside of the human subject. The contraction of the disease from contact with infected objects may constitute a source of error and obscure the proper estimation of the infectious period.

There can be no question that at the very beginning of scarlatina the contagiousness is limited. We have frequently known children, exposed to the disease at the very outset, escape infection only to contract it when re-exposed a number of weeks later. Children who are immediately separated from a case of scarlet fever as soon as it is discovered will frequently remain well; in this respect scarlet fever differs strikingly from measles, in which disease the contagion is extremely active even before the appearance of the rash.

Scarlet fever is highly contagious during the period of eruption and

¹ *Pathogénie de la scarlatine.* Paris, 1895, p. 126.

usually for some time following the disappearance of the rash. The view has been generally held that contagiousness persists throughout the entire stage of desquamation, and that the infectious principle is resident in the epidermal scales. There have always been some dissenters from this view and the doubt as to the contagiousness of desquamating epithelium is becoming more generally entertained.

Scarlet fever is not only contagious before desquamation begins, but not infrequently after it has completely terminated. It is obvious, therefore, that the infection must reside somewhere in the body apart from the cutaneous surface. Experimental and clinical evidence both point to the throat and adjacent cavities as the probable lurking places of the infectious organisms. It is, therefore, of importance to continue the isolation of patients until discharges from the nose and ears have ceased.

It is probable that the prolonged infectivity manifested by certain cases of scarlatina is due to the presence of the scarlatinal contagium in the secretions of the throat or in the nasal and aural discharges.

It is practically impossible to state just at what period a case of scarlet fever ceases to be infectious. The more remote the time from the onset of the disease, the greater is the likelihood of the infection having been extinguished. Probably for this reason the isolating of the patient for the full period of desquamation has been found to be a good working rule.

Physicians connected with scarlet-fever hospitals not infrequently see patients who have remained in the hospital from eight to twelve weeks, give rise, upon their return home, to other cases in the same household. And this occurs despite the most careful disinfection of the body and the clothing.

These *return cases* occur in the experience of many hospitals in from 2 to 4 per cent. of the patients. We have seen patients at the end of eight, nine, ten, and eleven weeks, after every vestige of desquamation had disappeared, give rise to the disease in others. In a case recently observed by us we learned that, after the dismissal of the child from the hospital, the ear began to discharge again; shortly afterward a second case developed in the family.

Some years ago the following sad case came under observation at the Municipal Hospital: A child with a well-marked scarlet fever came to the hospital at an early stage of the disease, the eruption just appearing. The patient remained in the hospital *nine weeks*. Desquamation had completely ceased. An antiseptic bath was given in a room disconnected from the hospital building, and the child was dressed in clean clothing. The patient had had a discharging ear which had gotten well, but during the last bath slight moisture in the ear was noticed. A few days after the child's return, the mother and two other children were brought to the hospital with scarlet fever. The attack in the mother was severe, the disease terminating fatally in a short time. The mother had been exposed to the child before the latter was first admitted to the hospital.

The Contagiousness of Desquamating Epithelium.—Almost thirty years ago Thomas wrote: “The contagiousness of the postexanthematic period is usually ascribed to the scales of epidermis which separate during the process of desquamation; but it seems to me that there is not the shadow of evidence to prove that the contagion is contained in them either exclusively or even chiefly; for it may be presumed that the contagion enters from the blood into all secretions and excretions of the patient. Volz, in fact, totally denies the contagiousness of the epidermal desquamation.”

Von Kerchnsteiner states that “the most favorable conditions for contagion exist during the stage of eruption and acme of the exanthem; the most unfavorable during desquamation.”

(This subject is more fully discussed in the chapter on treatment.)

There is no evidence to indicate that the scarlet fever contagium is disseminated by *aerial transmission*. The immediate vicinity of scarlet-fever hospitals appears to be as free of the disease as other sections of the city. In this respect scarlet fever differs from smallpox, in which disease the territory immediately surrounding the hospital is apt to show a disproportionately large number of smallpox cases.

The following figures are taken from the *Medical and Surgical Reports of the Boston City Hospital*, 1897:

Radius of one-eighth	of a mile from scarlet-fever hospital	0 cases.
“ “ one-quarter	“ “ “ “ “ “ “	66 “
“ “ one-half	“ “ “ “ “ “ “	71 “
“ “ three-quarters	“ “ “ “ “ “ “	75 “
“ “ one	“ “ “ “ “ “ “	72 “
Within one mile of the hospital		286 “
Beyond the one-mile limit		756 “

It is seen from the above figures that no cases developed within the one-eighth mile limit about the hospital.

Our experience at the Municipal Hospital would lead us to believe that the striking distance of scarlet fever is extremely limited.

It has been exceedingly rare for families in the immediate vicinity of the hospital to become attacked with scarlet fever, although they have not escaped smallpox.

The fact that scarlet fever is not carried beyond the confines of the hospital walls rather militates against the view of the infectivity of scales, for in a scarlet-fever ward the air contains myriads of minute particles of desquamating epithelium.

Scarlet-fever Infection in Milk.—The transmission of the infection of scarlet fever in milk has attracted the attention of physicians for some years.

Thomas, writing in 1875, referred to two epidemics reported by Bell and Taylor in which the dissemination of the disease was ascribed to infected milk. In the latter epidemic one of the first cases of scarlatina occurred in the family of a milkman whose wife milked the cows. The milk was supplied to twelve families, in six of which scarlatina appeared in rapid succession, without contact with the milk server, and at a time

an the disease was not epidemic. The milk had been kept in a can in which scarlatinous patients had been treated.

'1886 Power' observed in London a severe epidemic of scarlet fever appeared to attack in particular the patrons of Hendon Farm, where cows were suffering from a peculiar malady. This disease was described by Klein,² who came to the conclusion that the animals were suffering from scarlet fever, and that the infection was conveyed in the milk to human subjects. The malady was introduced among the cows by an animal which had elevation of temperature, cough, faucial and nasal catarrh, a red rash about the eyes and on the inside of the mouth, followed two weeks later by desquamation and loss of hair. Pustules were present upon the udders, which later gave rise to milk abscesses. The animal had recently given birth to a calf. Klein found streptococci in the serum from the vesicles which he inoculated into a child. He likewise found streptococci in the blood of some scarlatina patients. This organism he regarded as the specific cause of scarlet fever.

In the same year Crookshank and Brown³ noted an epidemic among cows analogous to that observed by Klein. After carefully studying the same and making further inoculations from an accidentally received sore on the hand of a dairyman, they proved that the disease was cowpox. The same streptococcus was obtained by culture.

In 1885 an epidemic of scarlet fever occurred in Rostock, Germany, apparently from milk infection.⁴ A very striking increase in scarlet fever occurred in June, in which month 36 cases developed. It was discovered that the families (with two or three exceptions) were supplied with milk from a farm in the village of Gehlsdorf, where 6 cases of scarlet fever and a number of cases of sore throat existed among the farmers' families and employes. Some of those who were taken ill had milked the cows and had handled the milk. According to the investigations of the Rostock physicians, 8 of the 36 cases could with certainty be attributed to infection from the milk. As indicating the presence of the infecting agent in the milk, it was noted that those who drank boiled milk escaped; this was the case in two children, two and four years of age, who remained free, although other children in the same household who drank raw milk contracted the disease.

Freeman⁵ has made a careful study of the transmission of various diseases through infected milk. He states there is conclusive evidence that contaminated milk has caused certain epidemics. In 26 recent epidemics of scarlet fever in England traceable to milk, 15 were found to be due to the disease in man.

Epidemics due to infected milk have within recent years been reported

¹ Milk Scarlatina, London. Report of the Medical Officer of the Local Government Board, February, 1885 and 1886, No. 8, p. 73.

² The Etiology of Scarlet Fever. Proceedings of the Royal Society of London, 1887, xiii.

³ Communication to the Pathological Society of London, 1887.

⁴ Quoted by von Jürgensen. Loc. cit., p. 413.

⁵ Medical Record, March 28, 1896. Quoted by Northrup in von Jürgensen's article on "Scarlet Fever." Loc. cit., p. 414.

in this country. In Plainfield, New Jersey, an epidemic was traced to a farm hand who had a mild attack of scarlet fever and who handled the milk during this time.

More recently an outbreak of scarlet fever occurred among 35 students of Purdue University, Lafayette, Indiana. The 35 cases were fed at eleven different boarding houses, all of which were supplied with milk by the same dairyman. Five private families supplied with the same milk had one or more cases of the disease in their households. The infection was attributed to winter clothing which had just been put on, and which had been laid away the March before, at which time the "dairyman's family ran through a course of scarlet fever."

From the now extensive literature upon the subject, we may conclude that scarlatina may be conveyed through a contaminated milk supply. The proposition is not proven beyond the peradventure of a doubt, but the chain of circumstantial evidence is so strong as to render this conclusion almost irresistible. It would, furthermore, appear that the milk is contaminated through contact with an individual suffering or convalescent from the disease. The view advanced by Klein that the cows themselves suffer from scarlatina remains unproven and is not generally credited.

Hall,¹ in reviewing the subject of milk infection, makes the following interesting statement: "While scarlet fever occurs in epidemic form in those countries where cows' milk forms a staple article of food, especially among children, it does not occur in countries where cows' milk is not used as a food, or where children are raised upon mothers' milk only." In Japan cows' milk is not used, and scarlet fever is practically an unknown disease there. In India, cows' milk is used, but children are kept at the maternal breast until they are three or four years of age. Scarlet fever is a rare disease in India, seldom occurring in epidemic form.

Pregnancy and the Puerperium.—It cannot be said that pregnancy increases the predisposition to scarlet fever, for, according to Senn, Tourtual, and Trousseau, no case of scarlet fever in pregnant women was observed by them during extensive epidemics of the disease. That scarlet fever is an excessively rare occurrence during pregnancy is evidenced also by the statement of Olshausen that he was able to find only seven cases in medical literature. When scarlet fever does complicate gestation it is prone to lead to abortion or premature delivery.

Great diversity of opinion is expressed, in the extensive literature² on the so-called *puerperal scarlatina*, as to the real nature of this affection.

Malfatti³ in 1801 published an account of a malignant scarlet fever epidemic which prevailed among puerperal women in confinement in Vienna. The symptoms were: offensive lochial discharge, abdominal tenderness, with later (between the second and seventh days after

¹ New York Medical Record, November 11, 1899.

² An admirable collation of the literature on this subject is presented by Marcel Durand in a Paris thesis entitled "Étude historique et critique sur la scarlatine puerpérale." Pp. 325. Paris, 1891.

³ Journal der prakt. Heilkunde, by C. W. Hufeland, Bd. xii., part iii. p. 120. Berlin, Ungar, 1801.

delivery) chills, headache, ringing in the ears, hot skin, nervousness, and moderately rapid pulse; then a diffuse reddish exanthem, which on the third, fourth, or fifth day became bluish, accompanied by marked nervous symptoms, failure of the vital powers, and death.

In 1875 Braxton Hicks read before the London Obstetrical Society a paper in which he stated that of 89 puerperal cases under his care that had febrile symptoms, he regarded 37 as suffering from scarlet fever. A few of these patients had an angina of any severity and 17 did not have an eruption. In 2 instances scarlet fever developed in children who were exposed to the puerperal women. In the discussion that followed, some endorsed but many repudiated the diagnosis of scarlatina in these puerperal fevers.

Olshausen¹ combats the contention of Hicks and mentions the argument which led Helm and subsequent writers in Germany to regard puerperal fever with scarlatiniform rash as puerperal septicæmia: (1) epidemics occur in maternities and not synchronously with general epidemics; (2) the malady has a malignity more in accord with puerperal septicæmia; (3) it is often complicated with peritonitis and other manifestations analogous to those seen in puerperal fever; (4) origin in the early days of the *post-partum* as is observed in septicæmia; (5) in the majority of cases it has been impossible to establish contagion.

Olshausen collected 141 cases of scarlatiniform rash occurring during pregnancy and the puerperium; these were reported by Koch (3), Schneider (5), Clemens (2), Simpson (2), Hardy (2), MacClintock (34), Brown (9), Johnston and Sinclair (2), Winkel, Halahan (25), Hicks (18), Lange, Denham (8), Senn (7), Dance (1), Trousseau (1), Gueinot (4), Hervieux (7), and Olshausen (5). Of this number only six occurred during pregnancy. Eight developed immediately after confinement, 62 from the first to the second day after confinement, 27 the third day, and 22 from the third to the eighth day afterward.

Winckel,² in expressing his incredulity concerning the scarlatinal nature of Hicks' cases, mentions the fact that lying-in women in England more frequently exhibit an erythema upon the cutaneous surface than in Germany.

Martin³ is of the same opinion and regards true puerperal scarlatina as a rare occurrence. Indeed, in 38,000 accouchements he observed this complication but three times.

Von Jürgensen, after a careful study of Malfatti's cases, does not regard them as true scarlatina, but as puerperal septicæmia. He believes that scarlatina, in the strict meaning of the term, is of slight significance as a factor in the mortality of the puerperium.

The fact is recognized that puerperal septicæmia may be attended with a rash which cannot be distinguished from that of scarlet fever. The lying-in woman may develop after confinement either a true *scarlet fever* or a puerperal fever with a *septic scarlatiniform rash*. There can

¹ Archiv für Gynäkol. und Obstet. de Credé, 1876.

² Die Pathologie und Therapie des Wochenbettes, third edition, p. 350. Berlin, Hirschwald, 1875.

³ Zeitschr. für Geburtsh. und Gynäkol., 1876, vol. II.

be no doubt that in the past many instances of the latter condition have been regarded as puerperal scarlatina. The differential diagnosis is often extremely difficult. The following points would indicate a puerperal infection rather than scarlet fever:

1. The absence of an epidemic of scarlatina and of any history of scarlatinal infection.

2. The presence of lesions of the genital tract, such as inflammation in and around the uterus. In puerperal infection metritis and peritonitis are more commonly found than in scarlatina after confinement.

3. In puerperal septicæmia the rash is often irregular. It may be circumscribed to the lower portion of the abdomen; in some cases it is morbilliform. When it is diffuse and scarlatiniform in character, the spread over the body is usually more rapid than in true scarlatina. Occasionally the rash may reappear even as often as seven times, as reported by Lucas-Championnière.

4. The associated symptoms seen in scarlatina are only imperfectly present. Angina is, as a rule, slight or absent; the strawberry tongue is not seen; renal complications are rare and desquamation is usually branny instead of lamellar.

5. The mortality is lower in true scarlatina than in puerperal fever with septic rash. Among the 141 cases collected by Olshausen, of fever and scarlatiniform rash occurring in puerperal women, the mortality was over 50 per cent.

In doubtful cases the history of a previous attack of scarlatina in the patient would constitute presumptive evidence against the existence of this disease.

It is important to bear in mind that in certain subjects the employment of intrauterine or even vaginal irrigations of bichloride of mercury may provoke the appearance of scarlatiniform rashes which may be regarded as septic or may be confounded with scarlatina.

Surgical Operations.—It would appear, from the rather convincing case of Prof. von Leube (mentioned on page 346), and from occasional epidemics in surgical wards of hospitals (such as that reported by Howse¹ occurring in Guy's Hospital), that the scarlet-fever poison may at times gain entrance into the system through wounds.

Furthermore, it is probably true that persons who have undergone a surgical operation have less resisting power to the scarlatinal infection than healthy persons. This view is held by Thomas, who says: "It really seems as if such persons, in consequence of their general condition, possessed a greater susceptibility to the disease."

The total number of cases of scarlet fever which developed during the course of twenty years among surgical cases in the great St. Ormond Street Hospital in London was 163. Sir James Paget in 1863, in a lecture given at St. Bartholomew's Hospital, referred to 10 cases of scarlatina which he had observed after operation.

In a boy upon whom a lithotomy had been performed, the rash of

¹ Some account of an epidemic of surgical scarlatina occurring in Astley Cooper Ward in 1878, with remarks. *Guy's Hospital Reports*, London, 1879, xxiv. pp. 44-462.

scarlet fever appeared upon the day after the operation. Paget noted the brevity of the period of incubation in these cases, 8 of them being three days. He thought it probable that the patients had received infection before the operation and that the manifestation of the disease would not have appeared so soon, or possibly not at all, if the patients had not been disturbed by operative interference.

Simovitch states that out of 2000 patients operated on in the Children's Hospital at St. Petersburg between 1897 and 1902, 44 had so-called surgical scarlatina. In 8 of the cases the period of incubation was less than twenty-four hours.

Wingrave,¹ in an exhaustive article on surgical scarlatina, reports 7 cases of scarlet fever occurring after circumcision.

Wingrave,² of Wurzburg, discusses the subject of rashes following surgical operations. Many of these are regarded by him as scarlatinoid erythematous rashes simulating scarlet fever. He believes, however, that he has seen cases of genuine scarlet fever develop after surgical operations. Inflammations upon the throat have not infrequently been followed by attacks of scarlet fever and by rashes simulating it. Lennox Browne states that "after removal of chronically enlarged tonsils, symptoms of pyrexia, rash, and desquamation, which are practically identical with scarlatina are exhibited occasionally."

Wingrave³ reports thirty-four rashes in patients operated upon for removal of tonsils and adenoids, during a period of seven years.

Fisher⁴ saw 3 cases of scarlet fever following the removal of the tonsils and adenoids. In 1 case the early symptoms were severe and were followed later by double otitis media and nephritis.

We have within the past few years observed 4 cases of scarlet fever after surgical operations. One followed circumcision, 1 an operation for deviation of the nasal septum, 1 an excision of cervical glands, and 1 after an operation for pyosalpinx.

We have also observed an attack of scarlatina following rapidly upon a burn. A colored child was admitted to the Polyclinic Hospital suffering from a deep burn of the face and arm. About twenty-four hours after admission the temperature rose to 105° F. and a scarlatiniform rash appeared upon the body. Nothing characteristic was observed in the throat or upon the tongue. The diagnosis was reserved, inasmuch as the symptoms might well have been attributed to an intoxication due to the burn. The child was isolated and a special nurse assigned to look after it. In about four days this nurse contracted a well-pronounced attack of scarlet fever.

Two distinct and separable conditions have doubtless been included in the term "surgical scarlatina." There can be no question that some of the rashes developing after operations represent the exanthem of genuine scarlet fever. On the other hand, a certain proportion, doubt-

¹ St. George's Hospital Reports, 1879, vol. x.

² Volkmann's Sammlung klin. Vorträge, 1886 and 1887, No. 29.

³ Tonsillotomy Rash. The Laryngoscope, 1901.

⁴ The Laryngoscope, May, 1904.

less, are toxic or septic scarlatinoid erythemas which are unrelated to true scarlatina.

The diagnosis should never be made upon the eruption alone, for a septic rash may be quite indistinguishable from that of scarlet fever. The general symptoms must be considered and the condition of the throat, tongue, glands, ears, and kidneys determined in order to throw the fullest light upon these difficult cases.

The diagnosis of scarlatina is sometimes indubitably confirmed by the unfortunate transmission of the disease to another subject.

THE SYMPTOMATOLOGY OF SCARLET FEVER.

Period of Incubation.—By the period of incubation is meant the time elapsing between the reception of the scarlatinal poison into the system and the first manifestation of symptoms of the disease. It is well to bear the fact in mind that the reception of the contagion is not invariably coincident with the exposure to the disease.

The breeding stage of scarlatina is briefer and at the same time more variable than that of the other acute exanthemata. Within its comparatively narrow limits, a considerable degree of variation occurs. The incubation stage of smallpox, although extending over a longer period, is strikingly uniform and reliable; to be sure, there are some variations, but these constitute exceptions. Measles, too, has a comparatively constant period of incubation.

The various writers on scarlet fever, in giving expression to their views as to the duration of the incubation stage, are guided largely by their individual experiences. Apart from actual differences in the clinical experiences of physicians, some of the widely divergent incubation periods may possibly be attributed to differences in the discriminating judgment of the observers. The more conservative writers are in general agreed that the most common period of incubation of scarlet fever is *between three and seven days*; the narrower these limits are contracted as a general proposition, the greater is the liability to error. Thomas regards "four to seven days as the most frequent interval," and looks upon shorter or longer periods as exceptions to the rule. Von Leube and Forchheimer both subscribe to this estimate. Vogl believes that the exanthem appears three or at most five days after infection.

While these intervals cover the vast majority of cases, there have been recorded occasional authentic instances of much shorter and longer periods of incubation. Trousseau's case of not more than twenty-four hours' incubation is of interest. He writes: "A London merchant had taken one of his daughters to the Faux Bonnes in the Pyrenees, and had passed the winter with her at Pau. On his way back to London he stopped at Paris, where he wished to remain some days. His eldest daughter was keeping house for him in London. Impatient to embrace her father and sister, she started for Paris. When crossing the channel, she was seized with fever and sore throat, and seven or eight hours later

arrived at Paris in the middle of a very serious attack of scarlet fever. She alighted at the hotel, almost at the very moment when her father and sister arrived from Pau. The two sisters remained together in the same room, and in twenty-four hours the sister who had come from Pau showed the first symptoms of a mild attack of scarlatina. In London the disease was then epidemic, but there were no cases at Pau."

Trojanowsky, Förster, Sörensen, Murchison, Alonzo Clark, Raven, Hagenbach-Burkhardt, and others have recorded periods of incubation of twenty-four hours or even less; so that it may be accepted that in rare cases the infection may give rise to symptoms almost immediately after entrance into the system.

As to long periods of incubation, there is much divergence of opinion. Veit claims it may be twelve to fourteen days; Paasch published a case in which it was twelve days; Gerhardt and Reinhold credited periods of eleven to thirteen days. Bawly records an instance of twenty-one days and Trojanowsky one of twenty-eight days.

Murchison, in his wide experience, has only been able to collect a series of 13 cases in which he could be sure of the incubation period; in not a single one of these cases was the period longer than six days.

On the other hand, Hagenbach-Burkhardt¹ reports 57 cases in which he has been able to study the incubation period. Of this group the remarkable number of 35 had incubation stages of over seven days. Under eight days there were 4 cases; nine days, 2 cases; ten days, 1 case; eleven days, 5 cases; twelve days, 1 case; thirteen days, 4 cases; fourteen days, 2 cases; fifteen days, 5 cases; seventeen days, 2 cases; eighteen days, 1 case; nineteen days, 2 cases; and over twenty days, 6 cases. This is certainly a most remarkable array of long incubation periods to come within the experience of any one observer.

Some of these instances and others exhibiting long periods of incubation may possibly be explained upon the grounds of a temporary immunity retarding the susceptibility to the scarlet-fever poison. While unprotected individuals are almost invariably susceptible to the contagion of smallpox and measles, the same is not true of scarlet fever. Certain individual conditions about which little is known seem to make some persons immune at one time and susceptible at another to the infection of scarlet fever.

We have recently had the opportunity of watching a protracted epidemic of scarlet fever in a home for children in this city. For a period of over three months, children contracted the disease two or three at a time and were sent to the Municipal Hospital. About 40 out of 100 were thus gradually attacked. It would seem that in many of the children the individual susceptibility was temporarily in abeyance or that the infection was not received by them in the beginning in sufficiently intense or concentrated form.

It is alleged by some writers that a virulent contagium may shorten the period of incubation, and that a similar abbreviation of this stage may result when the scarlatina occurs in a surgical or puerperal subject.

¹ Ueber Spital Infectionen, Jahrbuch für Kinderheilk., Bd. xxiv. p. 305.

Holt¹ has tabulated records of the incubation period in 113 cases, some of which were observed by him, but most of which have been abstracted from the literature of the subject:

INCUBATION PERIOD.

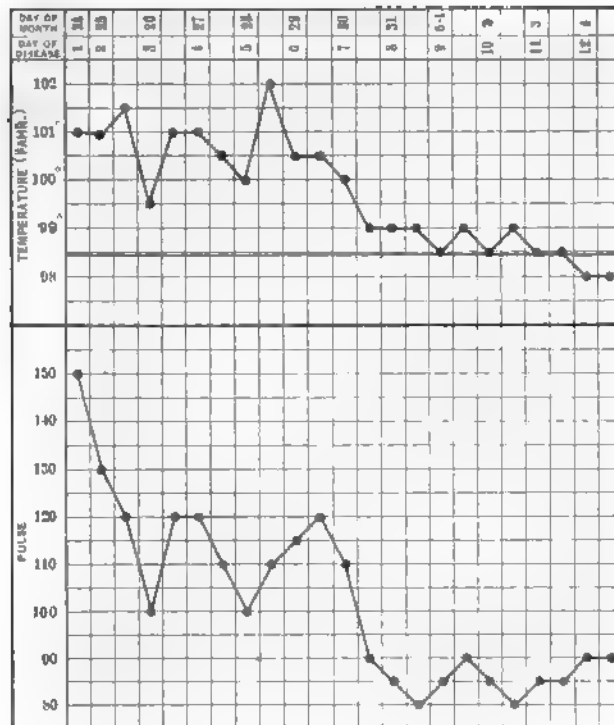
24 hours or less	6 cases.	7 days	8 cases.
2 days	15 "	8 "	2 "
3 "	28 "	9 "	5 "
4 "	25 "	11 "	1 case.
5 "	6 "	14 "	1 "
6 "	15 "	21 "	1 "

It is seen that in 87 per cent. of these cases the incubation period was between two and six days.

Simple, Usual, or Normal Scarlatina (Scarlatina Simplex).

Period of Invasion.—During the stage of incubation no symptoms, as a rule, are present, the morbid process being entirely latent. The

FIG. 50



Temperature and pulse record of scarlatina simplex. J. B., aged six years; mild case of scarlet fever terminating in recovery.

onset of the disease is sudden. The earliest symptoms are: indisposition, fever, headache, vomiting, and sore throat. Chills are usually absent

¹ Diseases of Infancy and Childhood, New York, 1896, p. 389.

in severe cases. In children *vomiting* is the earliest as well as the most prominent of the invasive symptoms, and is, therefore, of suggestive diagnostic import. Not infrequently children in the full bloom of the disease are quite suddenly seized with vomiting rapidly followed by other symptoms of scarlatina. Billington observed this symptom in 80 per cent. of his cases. We have obtained a history of the occurrence of emesis in 76 out of 155 cases, or about 50 per cent. We find that the average frequency of this symptom is greater than would be indicated by these figures. The evacuation of the contents of the stomach may be accompanied by diarrhoea, although usually the bowels are constipated. In severe cases in infants convulsions are not uncommon. There is loss of appetite and the tongue is furred. Adults and older children who are able to appreciate the sequence of the symptoms often indicate sore throat as the first.

Temperature.—The temperature rises rapidly, often reaching 102° or more in the course of a few hours. The pulse increases in frequency and, compared with the temperature, is often disproportionately rapid. The radial pulsations may number in children 140 to 160 per minute, and in adults 120 to 140.

Headache and vertigo are common, and the patient may be alternately somnolent and restless. The thirst is often intense. The patient is usually prostrated and presents the facies of a very sick person. The mouth is hot and dry, the eyes dull and listless, and the face flushed.

The fever in scarlatina is subject to great variations, being influenced by the severity of the epidemic and the nature of the accompanying complications. The pyrexial curve is by no means as constant as is seen in the other two important exanthematous diseases—smallpox and measles.

Wunderlich¹ gives the following as the average febrile course: The temperature at the onset of the disease rises rapidly, and after a few hours reaches 104° to 105° F. or higher. With slight morning remissions the fever still increases from the appearance of the eruption until its complete diffusion over the surface. When the eruption has reached its height, the temperature begins to decline by gradual steps, with slight evening exacerbations.

It is thus seen that the fever is a continued one during the invasive and early eruptive period, and that the pyrexia subsides by lysis concurrently with the fading of the exanthem.

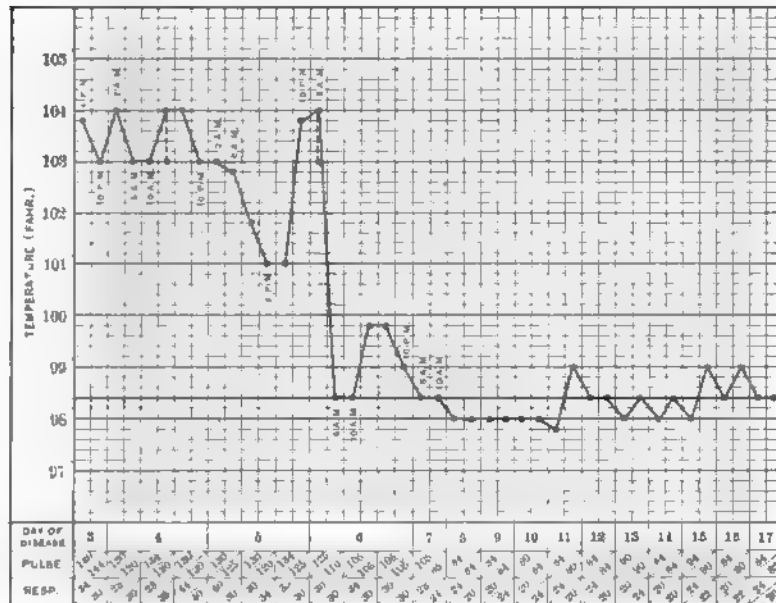
In well-pronounced cases of what might be called the normal form of scarlet fever the early rise of temperature is seldom below 104°, and it not infrequently reaches 105° or 106° F. The high temperature persists ordinarily for four or five days and then a decline sets in.

The intensity and the duration of the fever depend much upon the type of the prevailing epidemic. We have determined the duration of the fever in 265 cases of scarlatina which we treated in the winter of 1902-03, at which time the type of the disease was distinctly mild.

¹ *Eigenwärme in Krankheiten.*

Temporary rises of temperature occurring late and resulting from recognized complications or sequelæ were not considered.

FIG. 60



R. B., aged seven years; case of scarlet fever with an intense rash and severe early symptoms, terminating rather unusually by crisis.

DURATION OF FEVER IN 265 CASES OF SCARLET FEVER TREATED AT THE MUNICIPAL HOSPITAL IN THE WINTER OF 1902-03.

lasting 1 day	2 cases.	lasting 15 days	5 cases.
" 2 days	3 "	" 16 "	4 "
" 3 "	17 "	" 17 "	3 "
" 4 "	19 "	" 18 "	1 "
" 5 "	32 "	" 19 "	2 "
" 6 "	40 "	" 20 "	3 "
" 7 "	35 "	" 21 "	0 "
" 8 "	29 "	" 22 "	0 "
" 9 "	22 "	" 23 "	1 "
" 10 "	14 "	" 24 "	0 "
" 11 "	14 "	" 25 "	0 "
" 12 "	10 "	" 26 "	1 "
" 13 "	4 "		
" 14 "	4 "		
		Total	265

It will be seen from the above table that in the largest number of cases the fever terminated upon the *sixth* day of the disease. In 158 cases, or 60 per cent., the fever lasted from five to nine days. It must be remembered that the prevailing form of the disease was mild and the mortality low.

Jamieson states that of 200 cases observed by him the maximum temperature was reached—in 11 cases on the first day, in 76 on the

second day, in 75 on the third day, in 36 on the fourth day, and in 2 cases on the fifth day.¹

Deviations from the pyrexial curve above mentioned not infrequently take place. Instead of declining by lysis the temperature may fall by crisis. On the third or fourth day a sudden decline of the fever to normal or subnormal may take place. The temperature may then continue for some days at or slightly above normal. Henoch, Fürbringer, and Jürgensen have described such cases and Litten has reported instances of high initial fever followed by an apyretic course. Henoch noted 4 cases out of 175 with normal morning temperature and evening elevation. Litten observed similar cases.

Ordinarily, high fever accompanies severe cases with well-marked eruptions, but there are numerous exceptions to this rule. Leichtenstein mentions a case with marked delirium and intense eruption running an almost afebrile course. Cases of a malignant type may be entirely unaccompanied by elevation of temperature, and, indeed, the temperature may even be below the normal line.

It is not rare for very mild cases to be *unaccompanied by pyrexia*. We recall an afebrile case developing in the hospital whose temperature record we were enabled to observe for several days before the attack.

Fürbringer² describes a *secondary fever* in scarlatina that is independent of and unaccompanied by any discoverable complication.

Wunderlich, quoted by Trousseau, observed a considerable elevation of temperature during the stage of desquamation. Gumprecht and Jürgensen have also recognized this secondary fever. Thomas³ describes irregular cases of scarlatina with protracted fever. He writes: "When the fever is irregular it fails to defervesce after the normal progress and disappearance of the eruption and angina, but continues for weeks, sometimes with the same intensity and a typhoid character like that of a variety of scarlet fever presently to be described; sometimes with increasing intensity, especially if it is to prove fatal, and at other times it declines gradually as in protracted defervescence. In such cases the pulse is often very rapid, the heart's action violent, and the first sound of the heart diffuse or even replaced by a distinct murmur." And, again, "Not infrequently there occurs still another form of the disease in which there are not only local affections of moderate, perhaps even trifling importance, but also disproportionately severe fever of long duration which characterizes this variety as a typhoid scarlatina." Thomas remarks that in these cases the fever is the chief symptom and that it may be protracted for weeks.

Hyperpyrexia is more frequently observed in scarlet fever than in the other exanthematous diseases. It is not so rare for 107° F. to be reached; such cases usually terminate fatally, although when the hyperpyrexia is not protracted recovery may take place. In rare cases the fever may mount to an extraordinary height. Wunderlich records a temperature

¹ Quoted by Forchheimer, loc. cit.

² Realencyklopädie, Bd. x., 5, p. 472. Quoted by Jürgensen, loc. cit.

³ Loc. cit., pp. 254 and 269.

of 110.3° F.; Thomas, 111.2° F.; Leichtenstein, 109° and 109.9° F., and Dr. Currie, according to Gregory, 112° F. These rises of temperature were, as might be expected, shortly followed by death.

Throat Symptoms.—Throat symptoms are, as has been stated, early complained of by adults. On inspection, general faucial redness is observed, involving particularly the uvula, tonsils, and soft palate. When the cutaneous eruption begins to manifest itself the redness increases and there develops œdema and swelling of the mucous tissues. At times a thin, grayish or yellowish film of exudate may be seen on the swollen tonsils. Often the soft palate, uvula, and buccal mucous membrane show a punctated redness similar to that later observed upon the skin.

The stage of invasion is brief, not lasting ordinarily more than twenty-four hours. In some cases the eruption appears before twelve hours have elapsed.

In a series of 84 cases of scarlatina, Barthez and Rilliet observed the eruption appear as the first symptom in 4; in the majority of the cases, however, the eruption manifested itself at the end of twenty-four hours. Trousseau saw a severe case of scarlatina with marked brain symptoms in which the rash was delayed until the eighth day. It is, however, distinctly exceptional for the stage of invasion to last much longer than twenty-four hours.

Stage of Eruption.—The exanthem of scarlet fever usually begins upon the neck and subclavicular regions, then spreading rapidly to the chest, face, abdomen, arms, and legs. A variable time elapses in different cases before the acme of the eruption is reached. The milder efflorescences reach their height earlier than those of greater intensity. In severe cases the rash may take until the third or fourth day before its greatest intensity is attained.

The *color* of the scarlatina exanthem varies in different individuals and is extremely difficult to depict in words. It has been variously designated by writers as scarlet, bright red, boiled-lobster tint, raspberry-juice color, rose colored, wine colored, etc. These terms are permissible because they convey a definite impression to the mind, but when these tints are compared with the exanthem at the bedside the terms are seen to be inaccurate. The color of any inflammatory eruption is due to the blood appearing through the texture of the skin. The amount of blood in the skin as determined by the calibre of the cutaneous bloodvessels, the character of the blood, and the complexion of the individual all influence the coloration. It is a matter of daily observation that the rash in fair-skinned persons is brighter than in those of swarthy complexion, whose skin contains a greater amount of epidermal pigment. In general, the scarlatinal rash is reddish, sometimes bright, but more often *dull or dusky red*. Sometimes the eruption is so brownish-red, particularly in dark-complexioned individuals, as to almost approach a bright terra-cotta color. More rarely the element of blue is so well marked, particularly in dependent areas of skin, as to be quite purplish owing to the venous congestion. The color varies not only in different

persons, but at different periods in the same individual. A bright eruption commonly becomes dusky before it fades.

When the scarlatinal exanthem is viewed at a little distance it gives the impression of a uniform reddish blush. When, however, the skin is closely scrutinized it is seen that it is made up of innumerable reddish points or puncta. These are of a deeper tint than the skin intervening between them.

At times eruptions are seen in which the skin between the puncta is of normal coloration. This appearance may occasionally be noted during the coming out or evolution of the exanthem. Ordinarily the points of greatest color intensity are surrounded by areolæ of somewhat brighter hue. When these coalesce, as is usually the case, a diffuse eruption is presented, the puncta being scarcely distinguishable through the obliteration of contrast. At times the areolæ are narrower, exhibiting a little intervening normal skin and giving the eruption a more or less *peckled* appearance. In other cases with larger pale areas a *mottled* appearance is noted. Finally, there may exist large, irregular patches of healthy skin, particularly on the arms, legs, and buttocks, producing so marked a *blotchiness* of the exanthem as to suggest a strong resemblance to measles.

The scarlatinal eruption frequently exhibits small pinpoint to pinhead-sized, reddish elevations, which occur most commonly at the sites of hair follicles. These are frequently seen upon the extremities, particularly the lower, but may also appear upon the trunk. This condition was called by the older writers *scarlatina papulosa*.

In addition to these elevations a general *goose-flesh* condition of the skin is not infrequently observed. This is best marked upon the abdomen and chest, and is characterized by numerous pinhead-sized papules bearing a close resemblance to the "*cutis anserina*" evoked in the normal skin by exposure to either extreme of temperature. These papules may be faintly red or of the normal skin hue. They differ from ordinary goose-flesh in that they persist usually for some days. At times this condition is so pronounced as to impart to the skin a "*nutmeg-grater*" feel and appearance.

In the older descriptions of scarlet fever one reads of the occurrence of sudamina at the height of the efflorescence. Inasmuch as during this stage the skin is hot and dry with no tendency to sweating, one would not expect to find sudaminous sweat vesicles. It is extremely common, however, to find in well developed rashes innumerable *miliary vesicles*. To this condition the term *scarlatina miliaris* or *scarlatina vesicularis* has been given. The vesicles are conical, epidermal elevations, pinpoint to pinhead sized (size of millet-seed), with turbid or lactescent contents, and usually disseminated, although occasionally occurring in groups. They are commonly situated on the abdomen and chest and to a lesser extent on the extremities. The region in which they are frequently most copiously present is the *mons veneris*, for here the erythema is often intense. In this region they are prone to develop into minute but well-marked, yellowish pustules.

Rarely, contiguous vesicles may coalesce, forming blebs of the size of a pea or larger, constituting the *scarlatina pemphigoides* of the older writers.

Miliary vesicles may be seen in nearly all well-pronounced scarlet-fever eruptions. They are much more frequent than is generally supposed, being often overlooked on account of their minute proportions. A magnifying glass will often bring them into view when they are not clearly perceived by the unaided eye. In perhaps 20 per cent. of all cases and 50 per cent. of well-pronounced eruptions, vesicles are readily

FIG. 61



Miliary vesicles with lactescent contents appearing about the axilla with the rash of scarlet fever.

visible if looked for; lesions of this size, however, do not intrude themselves upon one's vision upon cursory inspection of the rash. The vesicles are more conspicuous in severe eruptions than in mild rashes. In decidedly exceptional instances they may be so pronounced as to overshadow the general scarlatinal exanthem and puzzle the physician in the diagnosis. Dr. J. P. C. Griffith, of this city, has reported several such cases.

Gee, Squire, Bohn, Rilliet and Barthez, D'Espine and Picot, Moizard, Baginsky, Vogel, and others believe that miliary vesicles are determined by an excessive degree of inflammatory action of the skin. Thomas, on

On the other hand, thinks that the miliary vesicles are produced by a position of the skin of patients. He states that in some cases this condition has been noticed so often and in such abundance that a miliarial eruption was observed only in a minority of cases. This coincides with the latter view. He cites cases in which miliarial eruptions accompanied mild scarlatinal rashes. He states it is perfectly possible in occasional cases to have the presence of a miliarial eruption cause decided difficulty in the diagnosis and lead to error.

From our experience with scarlet fever we have found miliarial vesicles to be more frequently associated with intense rashes than with mild ones, although they may occasionally be seen in the latter.

Some writers seemed to think that this miliarial eruption accompanied epidemics of scarlatina, and they fancied that these "epidemics" represented a peculiar infection rather different from scarlet fever.

During the period of the fading and decline of the eruption, pea-sized subcutaneous elevations are often noted. These are whitish papules containing the contents of which have been absorbed, for if ever, it is discovered fluid in them. They may be readily punctured with a needle, and resemble pea-pods. The exfoliation of the scales of these lesions and the desquamation of the miliarial vesicles constitutes a process at this will be later referred to. The course of the eruption varies somewhat. In some cases the face remains entirely pale, while in others it is commonly the temples and forehead that are flushed.

The seat of a deep redness is probably that this flushing is often associated with the true rash, for it is not rare to see the face desquamate profusely. The forehead often shows redness, but this is usually less intense than on the lateral aspects of the face. The tip and alae of the nose, and the upper and lower lips and the chin, commonly appear preternaturally pale. This *circumoral pallor* defined by the marked flushing of the cheeks gives the patient a most curious appearance, which, if not peculiar to, is always strongly suggestive of scarlet fever.

On the arms and legs the rash exhibits no peculiarities save its likelihood to early involve the flexures of the joints (groins, popliteal spaces, and elbow flexures), and its greater tendency to be blotchy. Upon the palms and soles the eruption is usually diffusely red without any puncta.

When pressure is made upon the scarlatinal rash a momentary pallor is produced, then a return of redness and finally a gradual paling again which persists for some minutes. We have seen on the legs pale bands persist where garters had previously been worn.

Indeed, one may inscribe a name upon the efflorescence with a blunt instrument and in a few moments note the white letters stand out upon the red background. This is the reverse of the ordinary dermographism and might be termed *anemic dermographism*. This is a vasomotor

¹ Scarlatina Miliaris, Jacobi's Festschrift, 1900, pp. 182-186.

peculiarity, but it is doubtful whether it possesses any reliable diagnostic value.

Itching is not infrequently experienced by scarlet-fever patients. While in most cases it is insignificant or entirely absent, it is occasionally quite severe. It may be noted during the early evolution of the eruption, at its height, or during the decline just before desquamation sets in.

In intense eruptions there is often some *edema* and *swelling* of the skin accompanied by an exaggeration of the lines of cleavage. The skin under such circumstances is thickened and shows wrinkling of the epidermis.

On the other hand, the eruption may be so *mild* as to make the diagnosis difficult and even impossible. Indeed, in rare cases the eruption may be absent altogether.

FIG. 62



Anger's bands at the sides of the garter during the height of a scarlet fever eruption. It is a vasomotor phenomenon similar to the white bands following digital stroking.

The eruption persists at its maximum intensity but for a brief period from a few hours to a day or two, and then gradually fades. Much variation is shown as to the entire duration of the exanthem; ordinarily the eruption lasts from *three to seven days*, but its life may be shorter or longer than this period. Cases doubtless occur in which the eruption is of such brief duration as to escape notice entirely; instances of scarlet fever without eruption, but followed by desquamation, are probably to be accounted for by evanescent undiscovered eruptions.

In some cases a temporary *fading or recession* of the rash occurs. It is not rare for the exanthem to be more vivid in color at certain times. The rash is not infrequently brighter in the evening than during the day. It is more rare for the eruption to recede completely and later reappear.

The Enanthem, or Mucous-membrane Eruption.—As has already been stated, sore throat is not infrequently among the earliest of the symp-

toms ushering in an attack of scarlet fever. In the very beginning there are commonly seen congestion and swelling of the tonsils, uvula, and soft palate. A punctated redness is often visible on the soft and hard palate. During the eruptive stage the gums and buccal mucous membrane usually exhibit some redness and swelling.

If the gums are inspected from the second to the fifth day there will oftentimes be seen *milk white patches* which look much as if they had been produced by the application of pure carbolic acid. These represent a desquamation of the epithelial covering of the gingival mucous membrane, and can readily be peeled off by slight friction. This process occurs at times in measles and perhaps also in other affections in which there is congestion of the oral mucous membrane.

The tongue is, as a rule, heavily covered with a grayish fur at the onset of an attack of scarlatina. Soon the tip and edges assume an angry, reddish coloration, and a roughened or granular appearance.

At this time also the fungiform papillæ on the dorsal surface of the tongue become swollen and prominent and peep through the surface coating. Usually by the fourth day or thereabouts lingual desquamation takes place and the coating is cast off, disclosing to view a red, raw-looking, often glazed surface studded with enlarged papillæ.

At times the papillary elevations are numerous and small, looking like the granulations in a wound. At other times they are scattered and more prominent. This condition of the tongue is of considerable diagnostic importance and has been variously described as the "raspberry," "strawberry," or "cat's tongue." It should be remembered, however, that mild cases of scarlatina occasionally exhibit no abnormality of the tongue whatsoever.

During the eruptive stage the condition of the throat undergoes aggravation. The tonsils are usually enlarged, reddened, and covered with a layer of mucus or actual pseudomembrane. The uvula, anterior pillars, and soft palate are intensely reddened and cedematous. The patient complains of much pain in the throat, particularly on swallowing.

Desquamation.—Exfoliation of horny epithelium begins during the decline of the eruptive stage. Desquamation occurs first upon those parts of the cutaneous surface which were first the seat of the exanthem. (Fig. 63.) Where the face has presented much eruption or even intense flushing a branny desquamation will often be noted as early as the fourth day. Almost simultaneously a similar epidermal exfoliation occurs upon the neck and the upper portion of the chest. This process is commonly inaugurated about the sixth or seventh day of the disease.

If one watches for the first evidence of desquamation on the trunk, it will be noticed as a number of discrete, pinpoint-sized, powdery scales. These represent the desiccated summits of the miliary vesicles. In a day or two these small scales are cast off, leaving minute, jagged rings of desquamation. The horny layer is now lifted off by centrifugal extension of these rings, which grow progressively larger. On meeting

PLATE XLIV.



So-called "Strawberry Tongue," showing the Enlargement of the Lingual Papillæ.

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PLATE XLV.



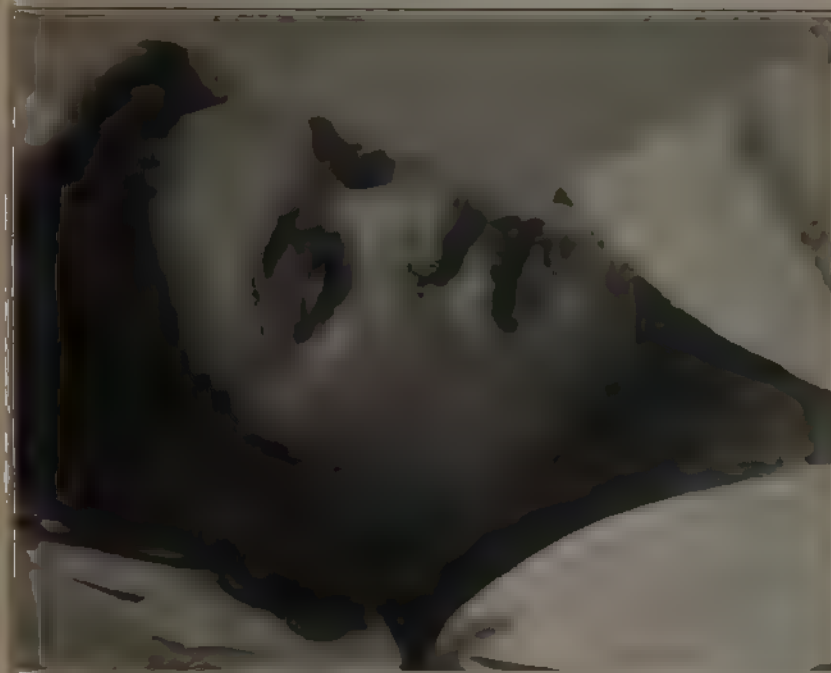
Desquamation upon Face, Neck and Chest.

Sixth day of the disease

enlarging rings of neighboring lesions they produce gyrate and geographic configurations resembling the contours of maps. In this manner the upper layer of the corneous stratum is removed. In some cases about the sixth or seventh day there develop on the trunk, as has already been stated (page 372), epidermal elevations which apparently contain air, and from which extensive desquamation starts. It would appear that the scaling on the trunk has its origin almost invariably in the miliary vesicles and in the air vesicles.

Upon the hands and feet the desquamation is of quite a different character. Here the horny layer is shed either in large flakes or more rarely *en masse*, with the result that a partial or complete epidermal cast is thrown off, resembling a glove or a slipper.

FIG. 63



Desquamation upon the face, 7th day of scarlet fever

It is seldom that these epidermal gloves remain intact until complete exfoliation, unless the hands are kept bandaged.

The most typical and characteristic scarlatinal peeling, however, is that which begins about the free border of the nail. Just beneath the edge of the nail a fissuring or cleavage of the horny layer takes place, the latter being stripped back toward the finger-tip, and thence up the finger. The peeled portion of the finger exhibits to view the new, soft, pinkish skin, whereas beyond is seen the harsh, horny cuticle. This desquamation originating in *subungual cleavage* of the epidermis is of

considerable diagnostic import; it is seen also upon the toes, but not so well pronounced.

Before desquamation begins upon the hands the skin becomes harsh, dry, and wrinkled. The occurrence of peeling may by attention to this condition be determined in advance.

In some cases, particularly when the rash is extremely mild, desquamation may be so slight as to be scarcely perceptible. Indeed, in rare cases it may be entirely lacking.

FIG. 64



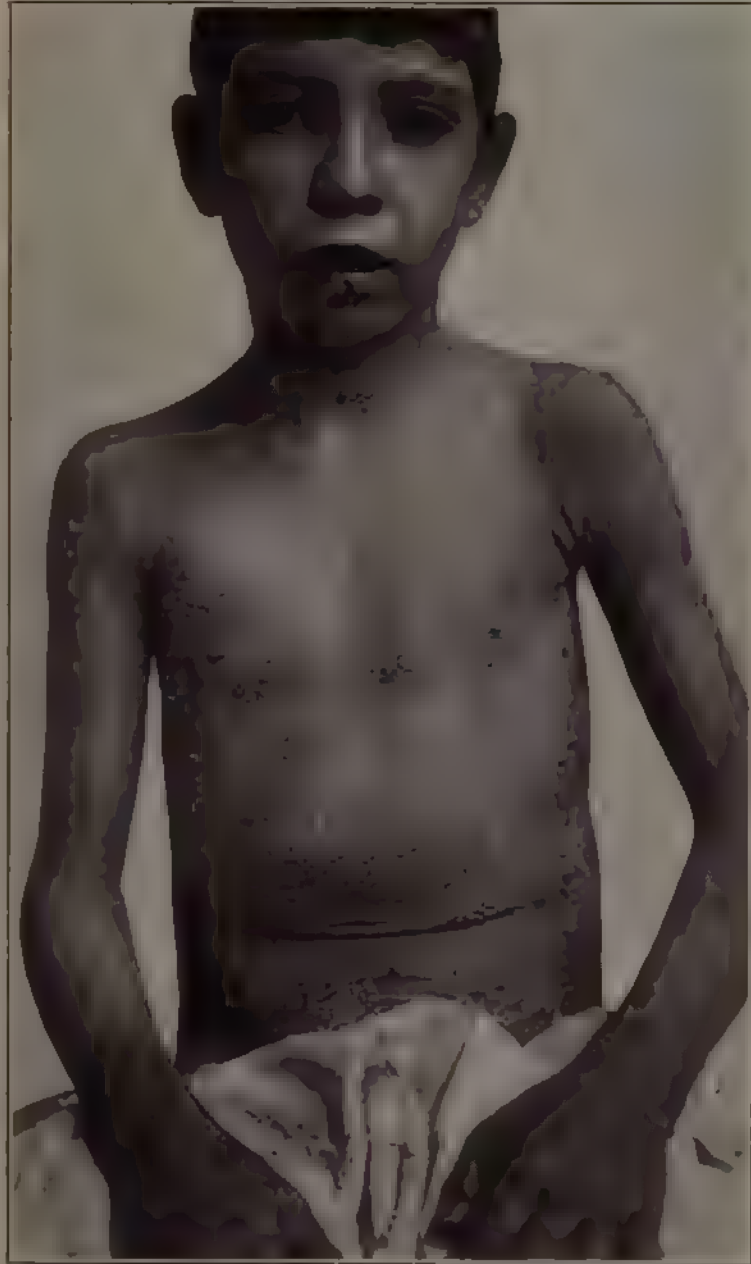
Unusually severe desquamation in a case of scarlet fever with an intense eruption. Enlarging scaling rings are well shown

On the other hand, it may be so intense as to resemble the affection known as exfoliative dermatitis. This is the form which is apt to be attended with exfoliation of large strips of epidermis and casts of the hands and feet. Other epidermal structures such as the hair and nails occasionally become affected, in which event the hair and nails are shed. Where the nails are not actually thrown off they may show a transverse furrow which in the course of time grows out to the free edge.

Duration of Desquamation. The duration of desquamation cannot be stated in definite terms, as it is subject to the greatest variation.

There are mild cases in which no desquamation can be detected after two weeks. On the other hand, severe cases, and even some mild cases,

PLATE XLVI.



Extensive Desquamation following a Severe Rash.
Ninth day of disease.

may continue to desquamate for eight, nine, or ten weeks. Indeed, where the rash has been intense a second and even third scaling may occur after the first desquamation has been completed.

Secondary desquamations are not particularly uncommon, although it is rare to observe the exfoliative process repeated more than a second time. When scaling occurs more than once the subsequent desquamations are, as a rule, not general, but limited to certain areas, particularly the palmar and plantar regions. The scales usually come away in the form of small or large flakes.

Thomas refers to a case of *Jadious* in which the scaling repeated itself five or six times. These repeated epidermal exfoliations protract the period of desquamation almost indefinitely. Scaling persists longest

FIG. 55



Well marked desquamation upon the dorsum of the hands and fingers.

on the hands and feet, particularly the latter. Our experience would lead us to say that the average duration of desquamation in well-marked cases of scarlatina is about six weeks.

The degree of intensity of desquamation is, as a rule, proportionate to the intensity of the eruption, but there are numerous exceptions to this rule. Many writers state that true scaling may occur upon parts of the body which have not been the seat of any exanthem. We prefer to believe that in these cases there has been a fugacious but unobserved eruption present. It is quite possible for a rash to be present during the hours of the night and, disappearing in the morning, completely escape observation. We cannot conceive of characteristic desquamation occurring without some previous vascular disturbance in the skin.

We recall the case of a ward maid who, after a few days' exposure to scarlatina, contracted a severe sore throat with fever, and who scaled profusely on the hands and feet, although no true eruption had even been discovered. It is, perhaps, nearer to truth to say that a rash was not seen rather than that it was not present.

If the skin is closely inspected distended cutaneous capillaries will often be found to be visible to the naked eye. It is not uncommon in intense rashes to note the presence of scanty, claret-colored, *petechial* extravasations into the skin. These are noted particularly in regions where the skin is thin and tender, such as on the neck, axillary folds,

FIG. 55.



Epiderma, glove like casts from a fatal case of scarlet fever

inner sides of the arms, flexures of joints, etc. These hemorrhages betoken intensity of the eruption rather than malignity of the infection. To be sure, in malignant cases the eruption may be hemorrhagic, but under such circumstances the extravasations into the skin are larger and accompanied by bleeding from some of the mucous membranes.

Lymphatic Glands. Intumescence of the lymph glands may be regarded as an almost constant accompaniment of scarlet fever. It would appear that the scarlatinal poison is responsible for the changes in the lymphatic structures, for not only are the subcutaneous lymph glands affected, but also the lymphoid elements of the liver, spleen,

intestines, etc. On this account Hawley has suggested that the term lymphatic fever be substituted for scarlet fever.

Quite early in the course of scarlet fever do we note an appreciable tumefaction of the subcutaneous lymph glands, more particularly those situated about the angles of the jaws.

The following presentation of the condition of the glands in 100 cases¹ will give an adequate idea of the extent of the lymphatic involvement in scarlet fever.

FIG. 67



Pronounced desquamation in large lamellæ

The various lymphatic glands were enlarged in the following proportion of cases:

Inguinal glands	100 per ct.
(a) pea-sized	23 per ct
(b) bean-sized	77 "
Axillary	96 "
Maxillary	95 "
Posterior cervical	77 "
Anterior cervical	44 "
Submaxillary	36 "
Epitrochlear	26 "
Sublingual	25 "

The inguinal glands were in the main enlarged to the size of a pea or bean, although occasionally they would reach the dimensions of an almond.

The epitrochlear glands vary from the size of a lentil to a pea. Not infrequently the enlargement occurred but upon one side. Occasionally there is a second enlarged gland just above the epitrochlear gland.

¹ A Clinical Study of the Lymphatic Glands in One Hundred Cases of Scarlet Fever, by J. F. Schamberg, *Annals of Gynecology and Pediatrics*, December, 1899.

The axillary glands vary in size from a pea to an almond. They are usually enlarged in clusters rather than singly.

The sublingual gland is scarcely ever larger than a lentil seed. The submaxillary lymphatic glands were found to vary in size from a pea to an almond. In one case a gland reached the dimensions of an orange, broke down, and suppurated.

The maxillary glands, or those just behind the angle of the jaw, reach the largest size of any of the lymphatic glands and are the commonest to undergo suppuration. In the above cases they varied from the size of a bean to that of an orange. The average was perhaps represented by the dimensions of an almond or hickory nut.

The anterior cervical glands, or those lying in front of the sternocleidomastoid muscle, were usually pea to bean sized, as were also those posterior to the muscle.

The glands were examined at various stages of the disease, as early as the second day, and as late as the fifteenth. In the cases studied upon the second and third days the glandular enlargement was so well marked as to suggest the probability that the glands are already somewhat tumefied on the first day of the illness.

The duration of the enlargement doubtless varies in different patients. In several cases, examined at intervals of a few days for three weeks, the glands were found to gradually diminish in size, but at the end of this time they were still slightly enlarged.

Statistics are frequently misleading, and those presented above are, perhaps, no exception to the rule. While it is true that the inguinal glands were enlarged in every one of the 100 cases of scarlet fever examined, it is more than probable that in some of them the enlargement antedated the attack of scarlet fever. The percentage of apparently healthy children with pea-sized or larger inguinal glands must be very considerable. Still the effort was made to eliminate this error as far as possible. It is in most cases not difficult to distinguish between an old and a recently enlarged gland. The former has a decidedly sclerotic feel, with the resistance, say, of cartilage. The latter presents a peculiar resiliency with the consistency of liver.

The enlargement of the glands about the jaw and neck is ordinarily proportionate to the amount and intensity of throat involvement. There are, however, occasional exceptions to this rule, and it should be recognized that extensive lymphatic swelling may occur with but slight throat symptoms.

When the glandular swelling is of moderate extent and of early occurrence, it usually undergoes gradual subsidence. When the swelling is very great, and particularly when it develops late, from the second to the fourth week of the disease, it is extremely prone to suppurate and form a glandular abscess. This will be further referred to under the subject of complications.

Respiratory Symptoms. Laryngitis.—Despite the intense inflammation of the pharynx in scarlatina there is but little tendency to involvement of the laryngeal structures. Trousseau's epigrammatic saying,

"Scarlatina has no liking for the larynx," is borne out by experience. He further remarks: "True scarlatinous sore throat, then, is pharyngeal, differing in this respect from the sore throat of measles, which is laryngeal, and from that of smallpox, which is both pharyngeal and laryngeal."

It is only when the inflammation of the throat in scarlatina is severe, with tendency to gangrenous change, and is accompanied by swelling of the surrounding connective tissue, that the larynx may become compromised. In such cases both the mucous membrane and the connective tissue of the larynx may undergo inflammation.

True, the larynx may become involved later in the course of the disease by the formation of ulcerations or the development of a pseudomembrane, which may or may not be due to the diphtheria bacillus.

Bronchial Catarrh.—In severe cases of scarlet fever a catarrhal condition of the bronchial tubes may be present even in the early stages of the disease. In malignant cases, that have proven fatal after an illness only of a few days, it has not been uncommon on autopsy to find an inflamed condition of the bronchial mucous membrane, with the presence of a mucopurulent exudate. Hensch,¹ Jürgensen, and others have recorded such cases. The former says: "The mucous membrane of the bronchi and the parenchyma of the lungs are excited by inflammatory influences far more frequently than we usually suppose. Not only catarrh, but more or less extensive bronchopneumonia, occurs in the first and second weeks of the disease. These conditions are frequently overlooked, however, because a whole series of synchronous, severe typhoid symptoms disguise them and divert the attention of the physician. We found bronchitis and bronchopneumonia in nearly all the severe cases, and also repeatedly during life."

Pneumonia either of the catarrhal or croupous variety is an uncommon occurrence in scarlatina; when it does occur it is usually in connection with severe cases of the disease.

Leichtenstern is authority for the statement that "in children acute lobar pneumonia, sometimes bilateral, and mostly involving the upper lobes, appears as well in the height of the disease as in the nephritic stage. These are pneumonias such as in the shortest space of time lead to a complete infiltration of a whole upper lobe, or more rarely a lower lobe."

Gastrointestinal Symptoms.—Vomiting occurs at the beginning of the disease in a large percentage of cases of scarlatina. In some severe cases the vomiting may continue for some days or may return after it has ceased. This may be accompanied by pains in the epigastrium. The *bowels* at the onset of scarlatina may be normal or constipated. In some cases, however, diarrhoea is present and in some instances it may be quite severe. In bad cases a persistent diarrhoea with greenish or bloody stools is often observed. This serves to increase the already existing weakness and prostration, and therefore adds to the gravity of the disease.

¹ Vorlesungen über Kinderkrankheiten, p. 642, third edition.

SCARLET FEVER

Nasal mucous membrane usually remains normal in scarlet fever. If the nose is involved it is usually the result of extension of a pyogenic infection from the throat. In scarlet fever of the anginose variety the mucous membrane of the nose may become reddened, swollen, and secrete a foul, mucopurulent, or bloody discharge, which excoriates the nostrils and adjacent portions of the skin. Ulceration of the mucous membrane may occur, occasioning the loss of considerable tissue.

The involvement of the nose is rare in simple scarlatina; it is much more common in the anginose variety.

It sometimes mentions a severe purulent rhinitis which develops early in scarlet fever. The profuse discharge from the nose is accompanied by a tremendous swelling of the cervical glands and suppuration. Occasionally extension of inflammation to the antrum or maxillary sinus occurs, as in a fatal case quoted by Roger. The streptococcus is taken upon as the cause of the purulent inflammation. We frequently observe purulent rhinitis in anginose scarlet fever.

The *mucous membrane of the lips* is commonly swollen and reddened. The covering is often lost, leading to superficial ulcerations which may bleed and become covered with crusts. The corners of the mouth may be fissured, the rhagades extending into the cheeks and causing considerable pain.

Scarlatina Anginosa—Severe or Septic Scarlet Fever.

This disease is characterized by an excessive development of the throat symptoms, but with particular severity of the throat manifestations. The aggravated nature of the attack is usually manifest from the outset. The incubative and invasive periods are usually short; with headache, chilliness and vomiting, the temperature rises suddenly to 104° or 105° F.; with the appearance of the eruption, which develops commonly within a few hours of the initial symptoms, the pyrexia may still increase until a burning fever of 106° or 107° F. is reached. The temperature in this form is not only higher than in simple scarlatina, but it is also of longer duration. The temperature during the first five or six days commonly fluctuates between 104° and 105° F., and then in cases that end in recovery declines by slow gradation in the course of two, three, or four weeks to the normal line.

The nervous symptoms are pronounced; delirium is commonly present, alternating with periods of somnolence or semicoma. At times jactitation with extreme restlessness and wakefulness are noted. With children there is persistent disposition to sleep, great irritability when awakened, and stubborn resistance against taking nourishment. There is not only complete anorexia, but also painful deglutition which prompts the patient to reject the proffered food.

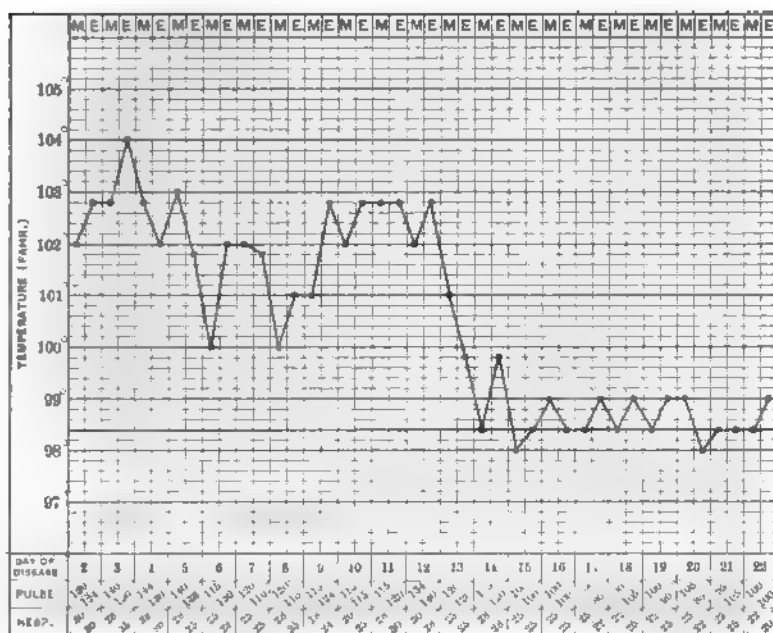
The rash is usually intense, covering the entire body, not excluding the face. Indeed, in bad cases the face often shows an intense deep-red, sharply margined, eruptive flush on the cheeks, which persists

for some days. The eruption is of vivid hue, at times acquiring even an erysipelatous appearance. In other cases the distribution may be irregular, the eruption occurring in patches upon the hands and feet, flexures of joints, buttocks, legs, etc.

In a fatal case in a child of eight months recently under our care, there were fiery-red patches on both cheeks, an intense erysipelatoid rash on the legs, and a faint punctate eruption on the trunk.

The pulse is rapid, frequently running between 120 and 150 per minute; it is likewise weak and compressible and often arrhythmical.

FIG 68



C. S., aged twenty-five years. Woman with the anginous form of scarlet fever, treated at the Municipal Hospital. Subsidence of temperature on the fifteenth day. Recovery.

The glands at the angles of the jaw become rapidly swollen; they commonly attain the size of a walnut or even a small apple. The surrounding cellular tissue participates in the general inflammatory process, producing great cervical intumescence and often causing the child's head to be bent backward.

Upon inspection of the *throat* the tonsils, arches, uvula, and soft palate are, during the first couple of days, seen to be intensely reddened and oedematous. Even at an early date there is a hypersecretion of a viscid, stringy mucus, which adheres to the tonsils and soft palate, and, becoming dry as a result of the mouth breathing, occasions much annoyance to the patient. Commonly by the third or fourth day a membranous exudate appears upon the tonsils, uvula, and soft palate,

extending often to the pharynx and posterior nares. The occlusion of the nasal channels further obstructs the ingress of air and distresses the already harassed patient. The buccal and alveolar mucous membrane is greatly congested, and often the seat of ulcerations from which blood oozes. The teeth, gums, and lips are covered with sordes, and an offensive, at times fetid odor is emitted from the mouth. The tongue is of an angry-red color and occasionally ulcerations, covered with a grayish exudate, are seen upon the edges. As has been stated, the nose discharges a purulent material and commonly shows ulcerations of the mucous lining. The eyelids may also become inflamed, the conjunctiva congested, and a purulent discharge issue from the palpebral cleft.

The child is often unable to swallow, water or milk being ejected through the nose. The nasal and faucial respirations are of a rattling character and painful to behold.

The extension of the morbid process along the Eustachian tubes leads to a purulent inflammation of the middle ear on one or both sides. Rupture of the tympanic membrane occurs with the evacuation of the purulent accumulation. The external auditory canals become infected by this discharge, and often develop ulcerations which may eat quite deeply into the tissues.

The child with a bad anginose scarlatina is a pitiable object—it lies with the head back to prevent the pressure of the swollen glands from compromising the breathing; the neck is greatly tumefied, the overlying skin stretched and glazed, the commissures of the mouth fissured and covered with blood crusts, the nose discharging a sanguinopurulent matter, the eyelids swollen, and the ears expelling a thin, ichorous pus. Indeed, every orifice of the face gives issue to a putrid and foul-smelling discharge, which contaminates the atmosphere about the patient with the stench. The general symptoms are those of a profound septicæmia.

In extremely bad cases, and in our experiences more particularly in mixed cases of scarlet fever and diphtheria, extensive ulceration and sloughing of the tonsils or soft palate may take place. The *necrosis* in such instances involves the entire thickness of the tissues, and leads commonly to perforation of the soft palate. We have in a number of cases seen these *perforating ulcers* of the soft palate; they may be bilateral, or occur only upon the one side. The accompanying symptoms are of a septic character, and the prognosis is unqualifiedly bad; death takes place in almost every case.

In fatal cases of anginose scarlatina death may occur as a result of the severe primary blood poisoning, or through the development of the later complications, such as nephritis, pneumonia, endocarditis, etc.

Bronchopneumonia is more frequent than is commonly believed, the symptoms being masked by the severe angina and the grave toxæmia.

The urine is diminished in quantity and nearly always contains albumin. The microscope will often discover the presence of tube casts and also red blood corpuscles.

A fatal termination is preceded by rise in the temperature to 106° or 107° F., an increasing prostration and stupor, and a progressive

weakening and augmented frequency of the pulse. Fatal cases usually succumb during the first or second week of the illness.

In severe cases of anginose scarlatina the lymphatic glands and adjacent tissues, under the influence of intense inflammation or, perhaps, a special infection, may undergo *gangrene*, leading to great sloughing and even alarming or fatal hemorrhage from the erosion of some large bloodvessel. Trousseau speaks of a case in a boy of fourteen "in whom the gangrene condition was so extensive that the muscles of the neck were dissected, as occurs in diffuse phlegmonous inflammations, showing the carotids pulsating at the bottom of a horrible wound."

In cases that end in recovery the temperature at about the end of a week or ten days begins to decline, the pulse slows and acquires better volume, the marked nervous symptoms gradually disappear, and the throat and adjacent cavities show a lessening in the intensity of the inflammatory process. The decline in the temperature is slower and less regular than in the usual type of the disease, and the normal is seldom reached before the end of the third or fourth week. Convalescence is apt to be complicated by nephritis and in some cases by rheumatism and endocarditis.

Scarlatina Maligna.

Malignant scarlatina, a fortunately rare form nowadays, is characterized by such a sudden overwhelming of the vital forces as to cause death in a few days, or, indeed, within twenty-four hours. The symptoms, consisting of extremely high fever, severe brain symptoms, and profound prostration, with or without hemorrhages into the skin and from the mucous membranes, develop with fearful rapidity, and the patient sinks under the dread influence of the poison.

The abruptness of the onset of the disease in these cases is remarkable. Children in the enjoyment of apparent perfect health may be smitten while at play. The child has a severe attack of vomiting, which may be accompanied by purging, and is followed by convulsions or stupor. The temperature rises rapidly to 107° or 108° F., the pulse to 140 or 150. Great restlessness and delirium may alternate with stupor. Excruciating headache and violent pains in the extremities are sometimes present.

The eruption is usually irregular, appearing often on the hands and feet before it is seen on the body. At times it appears only about the flexures of the joints. The rash may recede after a brief presence, only to appear a few days later. It is sometimes partial, assuming an erysipelatous aspect on the face or legs. It has commonly a livid hue, being beset with petechiæ and vibices.

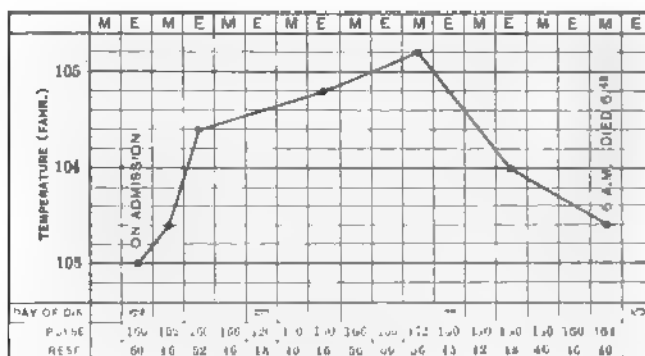
The local symptoms in malignant scarlatina are severe. The throat is so intensely swollen that swallowing is often impossible. The glands are greatly enlarged, and, if the patient lives long enough, the nose and middle ear become involved.

Prostration and collapse may occur so suddenly that *no eruption*

appears. The skin is pale or livid, the lips blanched, the eyes glassy and sunken with partial closure of the lids, the surface cold, the pulse weak and fluttering, and death imminent and inevitable. This choleraic type at times cannot be diagnosed without the presence of other cases of scarlet fever in the same household.

These rapidly fatal cases are rare, but well-authenticated instances are recorded. Morris¹ speaks of a child that was taken out apparently in perfect health for its morning airing and brought back within an hour with stupor and general muscular relaxation, cold surface, feeble pulse, and total insensibility; death occurred in twelve hours. Within a few days two other children in the same family were seized with scarlet fever which ran a regular course. Dr. Rush reported "a few instances of adults, who walked about, and even transacted business, until a few hours before they died." Such a case is mentioned by Morris: "A judge

FIG. 60



W. R., aged three years. Case of malignant scarlet fever with high temperature, dying upon the fifth day of the disease.

of one of the courts was seized with nausea while on the bench and retired to his home, where for two days he remained, scarcely willing to admit himself to be sick, and reluctant to confine himself to his chamber, though the rapid, feeble pulse and an imperfect eruption too plainly indicated the nature of the affection; on the third day he died while in the act of shaving himself." A near relative stood beside the corpse and contracted a similar fatal illness.

Gregory² in referring to malignant cases says: "In some extreme cases . . . all the ordinary appearances of scarlet fever are masked; petechiae, coma, and a sloughy state of the throat alone appear." And further he remarks there are cases "where no affection of the skin takes place at all." As an instance thereof he attended a woman and two grown-up daughters, in all of whom "the nervous system was utterly prostrated, or in the state of collapse. There was no violence, no delirium, no struggling for breath, no rash; but the pulse was small,

¹ Pathology and Therapeutics of Scarlet Fever, Philadelphia, 1858

² Loc. cit.

the skin cold, and the whole system depressed by the intensity of the poison. . . . They sank one after the other, without any attempt to rally. It was difficult to believe the disease scarlatina, but the eldest son took it in the usual form, recovered, and put the matter beyond doubt."

Hemorrhagic Scarlatina.—Another form of malignant scarlet fever remains to be described, namely, hemorrhagic scarlatina. This type of the disease is ushered in by high fever, severe prostration, and marked brain symptoms. A dusky-red erythema, usually imperfectly developed, is seen upon the skin and is soon followed by the appearance of scattered wine-colored or purplish, pinhead and larger sized petechiæ, and later ecchymoses. As in hemorrhagic smallpox, bleeding occurs also from the various mucous membranes, the nose, mouth, intestines, kidneys, etc. Epistaxis and intestinal hemorrhages are the most frequent and serve to exhaust the vitality of the patient. Vomited matter may show the presence of blood and thus early indicate the malignant character of the attack. The presence of blood in the urine may result from renal hemorrhage or oozing lower down in the urinary system. Women may bleed profusely from the uterus. If the patient escapes the blighting influence of the high fever and intense toxæmia he is pretty sure to be prostrated by the hemorrhages from the mucous membranes, or leakage into the brain or the other viscera.

The condition of the throat and lymphatic glands is, in bad cases, similar to what is encountered in the anginose form. These cases are almost invariably fatal; the pulse becomes feeble and rapid, the respirations quick and shallow, and the patient lapses into a terminal coma.

The occasional reddish hemorrhages into the skin which accompany intense eruptions in well-marked attacks of normal scarlet fever, and which are particularly seen upon dependent portions of the body, such as the back, should not be confounded with the malignant hemorrhagic form just described.

Thomas¹ calls attention to an irregular form of scarlet fever in which, with very moderate or trifling local symptoms, there occurs a severe protracted fever. This has been designated *typhoid scarlatina*, although no real connection with true typhoid fever is suggested. The protraction of the fever for three, four, or more weeks may be wholly, partially, or not at all attributable to local complications. At the outset there are marked cerebral symptoms, severe headache, delirium, somnolence, and great thirst. The eruption comes out promptly, but is often poorly developed, the same being true of the throat symptoms. Desquamation occurs, but the skin remains hot and feverish. Later the patient becomes apathetic and very deaf without accountable ear trouble; there is enlargement of the spleen, pulmonary congestion, and diarrhœa. Apart from the glandular enlargement, there are no local complications, and one is at a loss to explain the remittent fever, which now continues for weeks. Nephritis may develop and cause a

¹ Loc. cit.

continued high fever, which may sink to normal with the subsidence of the renal complication. Typhoid cases of this character that come to autopsy usually show—besides the usual scarlatinal changes—congestion of the meninges and brain, catarrhal inflammation of the respiratory organs, hypostases of the lungs, effusions into the serous cavities, splenic and hepatic enlargement, swelling of the mesenteric glands, prominence of the follicles of the small intestines, and even some tumefaction of Peyer's patches. In some of these cases, according to Thomas, a peculiar secondary scarlatinal eruption develops which differs from the first in that it is not a diffuse erythema, but of the nature of a *roseola*. The lesions are generally of a dark, rather scarlet-red color, at the same time smaller and less sharply defined, generally closer together, and less elevated above the surrounding pale skin than is the case in measles. The eruption may occur only on the face and extremities, or may be copiously distributed over the body to an extent even as to render the macules confluent. The rash may disappear in twenty-four hours, or may remain several days. It is followed by an intense lamellar desquamation. There is a concomitant congestion of the throat, some renewed tumefaction of the glands, and the lingual papillæ again become enlarged. Thomas considers this eruption as an irregular form of scarlet fever, and looks upon its development in the light of a pseudorelapse. This curious complication is not of grave import, as most of the patients recover.

Irregular or Aberrant Scarlatina.

The symptoms described under the title of *scarlatina simplex* may be considered as representing the usual or normal manifestations of scarlet fever. The anginose and malignant varieties are, in a sense, deviations from the classical form, and, therefore, irregular. In addition there occur from time to time, in connection with the more important symptoms, phenomena which have given rise to the term *irregular scarlatina*.

Irregularities of the Fever.—Cases of *scarlatina* accompanied by extremely high temperatures, reaching 107°, 108°, 110° F., have already been referred to. Such hyperpyrexia usually indicates malignancy and a fatal termination. The *protraction of the fever* for weeks has also been mentioned in connection with the so-called typhoid *scarlatina*.

Scarlatina may, in rare cases, occur *without fever (scarlatina sine febre)*. It is not uncommon to encounter very mild cases in which the temperature, after a brief and moderate rise for a day or two, sinks to the normal and remains so. Such cases may present all of the usual symptoms, but in a very moderate form.

In a series of cases reported by McCollom, 37 had temperatures not exceeding 99° F. It has been doubted that true *scarlatina* occurs without any rise of temperature whatsoever. Wunderlich¹ expresses this doubt in the following terms: "Whether among these abnormally mild cases there also occur those in which the temperature shows abso-

¹ Das Verhältniss der Eigenwärme in Krankheiten, Leipzig, 1870, p. 336.

lutely no change I cannot say from my own experience, because I have never been able in very light cases to observe the beginning of the disease." Von Jürgensen mentions 2 cases in his practice in which there was practically no fever. In 1, in a child of three and a half years, with a well-marked scarlatina, the temperature was below 98° F. during the entire illness, with the exception of one or two occasions, when it momentarily rose to about 100° F. In a second case also the temperature never rose above 100°.

We have recently had under our care a child with scarlatina which developed in the hospital and in which we were enabled to watch the temperature record for four days preceding the attack. M. S., aged nine years, was admitted to the scarlet-fever ward of the Municipal Hospital from a foster home in which there was an epidemic of scarlatina. The patient had on admission (January 10, 1903) such indefinite symptoms as to scarcely permit the diagnosis of scarlet fever. On January 14th, four days after admission, she vomited and a well-marked scarlatinal rash appeared over the entire body. At this time her temperature registered 99° F.; on the 15th and 16th it declined to normal and then to 98°; rising to 100° F. on the 17th, and then again falling to normal.

Irregularities of the Eruption.—The scarlatinal eruption may depart from its usual appearance and present atypical features. An excessive development of the miliary vesicles to such an extent as to mask the character of the eruption has already been referred to.

Partial Eruptions.—In some very mild cases the exanthem may be *poorly developed and limited* to certain regions of the body. The associated fever and angina are often correspondingly slight. Gregory saw cases in which the exanthem appeared only on the thighs. Thomas speaks of cases in which it is limited to one side of the body, or the upper or lower half of the body, or the lower extremities. Glaser describes a form in which the exanthem appears as a broad band around the neck or around the joints. Wildberg also noted it in the latter situation. Zehnder¹ observed it in the form of red spots scattered over the body.

In exceptional instances the face may remain entirely free of eruption. This is more apt to occur in mild cases in which the eruption is of only moderate intensity.

The scarlatinal exanthem is sometimes of an intense hue and accompanied by considerable swelling of the skin and even subcutaneous tissue, imparting to the condition an almost erysipelatous appearance.

Poorly developed eruptions are not always indicative of benign attacks, for the exanthem is sometimes *partial* in severe and even malignant cases of scarlatina. Morris² says: "It is by no means unusual to meet with cases where all the constitutional symptoms are well marked, though the eruption is confined to the wrists or flexures of the joints, and is there limited to a small number of *red points* only. I have met with many such in families where other cases were well marked. They are frequently fatal."

¹ Quoted by Thomas, loc. cit.

² Loc. cit.

Malignant cases are often characterized by irregularities in the time of appearance, duration, and character of the eruption. The latter is often blotchy, like the eruption of measles; in other cases it is purplish and at times hemorrhagic.

Scarlatina Sine Eruptione, or Scarlatina Sine Exanthémate.—The eruption of scarlet fever is its most conspicuous manifestation, and is commonly the symptom which leads to the diagnosis of the disease. There is general accord among writers on this subject that scarlet fever may, in rare cases, occur *without an eruption*. In malignant scarlatina death sometimes occurs so quickly that there is scarcely time for the exanthem to appear. The diagnosis in such instances must be confirmed by etiological evidence.

Apart from these cases the estimation of the frequency of *scarlatina sine exanthemate* depends much upon one's comprehension as to what constitutes scarlatina.

Nurses and physicians who are in attendance upon scarlet-fever patients, and the adult members of a household in which the disease exists, commonly contract a sore throat and fever. This condition has been termed *angina scarlatinosa*, or *scarlatina faucium*; it presents usually the same symptoms as are observed in follicular tonsillitis. These sore throats occur both in individuals who have never had scarlatina and in those who have at some time experienced the disease.

To assume that all of these cases represent instances of scarlatina without eruption would, we feel sure, be unwarranted; to assume that they are all non-scarlatinous would be, perhaps, an equal deviation from the truth. In the present state of our knowledge it is unwise to express one's self with any degree of dogmatism upon this question. The discovery of the specific cause of scarlatina would shed a flood of much-needed light upon these cases.

Bohn conservatively expresses himself as follows: "In the vicinity of a scarlet-fever patient, febrile indisposition, angina, and catarrh of the mucous membranes, vomiting, even diphtheria of the tonsils, in the other members that have already had the disease are almost daily occurrences. We must only accept a case as one of scarlatina, if, during an epidemic, especially in families where either early or late a distinct scarlatinal case appears, cases occur in which nothing more is lacking from the fully developed picture than the confidently awaited exanthem."

Mayr¹ states that the expression "scarlatina without eruption" is only justified in those cases in which the exanthem is absent, but in which we have otherwise typical attacks with fever, angina, and desquamation, and in addition etiological evidence.

Thomas² says: "A slight or moderately severe fever of short duration, accompanied by some pain in the neck and enlargement of the cervical glands, is not an uncommon occurrence in persons who have but little predisposition to the disease, especially if they be of mature years, and also in those who have already had scarlet fever in childhood. These

¹ Scarlatina. Hebra's Diseases of the Skin, English translation, London, 1866

² Loc. cit., p. 251.

symptoms are the more suspicious if scarlet fever has occurred in the family, or if the patient has probably been exposed to the poison. If the throat be examined, the characteristic redness is seen in a mild form, with or without a moderate enlargement of the tonsils; perhaps also the tongue presents the appearance of the scarlet-fever tongue. There are also malaise, anorexia, headache, and other symptoms of slight importance. Such attacks generally disappear in a few days, but they should receive the same attention which is paid to the unmistakable disease. *Every throat affection during a scarlet-fever epidemic is suspicious.*"

That some of these sore throats are cases of true scarlatina faucium is evidenced by the fact that genuine scarlet fever is occasionally contracted from persons suffering from this variety of the disease. Morris¹ records such a case: "The wife of a medical friend of mine, who was aiding in the care of the children of a relative, was seized with this modified affection and communicated scarlet fever in all its integrity to her own children."

Graves² refers to a boy who was taken home from a school where scarlet fever was prevailing; he complained of pain on swallowing, slight headache, and nausea. The next day the tonsils were swollen and there was increased pain on swallowing; the pulse was sharp, the skin hot, but there was no trace of eruption. These symptoms continued three days and then disappeared. Before the boy had completely recovered, his father and two sisters took scarlatina.

Trousseau, Graves, and others have reported cases occurring in scarlatina households in which *anasarca* without previous eruption has been the symptom to attract attention to the patient. Trousseau remarks: "I came to the conclusion that the persons who had only had eruption and consecutive anasarca, those who had only had anasarca, and those who had only had sore throat, had all had scarlatina, the affections seen in all of them being manifestations of that disease."

Thomas refers to cases in which the scarlatinal nature of the disease is proved by the subsequent occurrence of the characteristic desquamation, even when there has been no previous trace of an eruption. We have already spoken of a case of a ward maid, in attendance upon scarlet-fever patients, who developed sore throat, enlarged glands, and well-marked desquamation without having had a discoverable rash. There was, on close inspection on one day, a faint flush over the chest, but no more redness than is seen at times in health. We believe that all patients who desquamate characteristically have had an exanthem. Desquamation is the terminal stage of certain vascular changes in the skin, and it is inconceivable that a patient should present well marked scaling without an antecedent eruption. To be sure, the eruption may be of extremely brief duration and may entirely escape observation.

Secondary Septic Erythema.—Occasionally in severe cases of scarlatina of the anginose variety, a dusky-red, maculopapular erythema

¹ Loc. cit., p. 85.

² Quoted by Trousseau.

is observed to occur in the second or third week of the disease. The eruption is most commonly seen about the extensor surfaces of the knees and elbows, although it is at times more extensive and may involve the face and a considerable portion of the surface of the trunk and extremities. This erythema usually persists for two or three days. It occurs in bad septic cases with purulent rhinitis, sloughing throat and discharging ears, and is of evil prognostic import. The discharging nose and blotchy eruption may excite suspicion of a superadded measles infection.

Reference has already been made to an extensive, secondary, dark-red, roseolous eruption, mentioned by Thomas and regarded by him as a pseudorelapse rather than an accidental complication.

Scarlatina Without Angina.—In many mild cases of scarlet fever the congestion of the throat is so slight that under other conditions the throat might not be regarded as deviating from the normal. Writers generally agree that in rare cases scarlatina may exist without any angina whatsoever. In those cases in which the sore throat is absent the eruption is usually poorly developed, the fever is very moderate, and the entire attack mild.

Bergé¹ reports a series of cases of puerperal and surgical scarlet fever in which there was *not the slightest involvement of the throat*. He believes that the angina in scarlatina represents the site of inoculation of the poison, and cites the above cases to show that infection may take place through other mucous membranes or wounds, in which event the angina may be absent.

Scarlatina Without Desquamation.—As a rule, the extent of the desquamation is proportionate to the intensity of the eruption which precedes it. There are, however, occasional exceptions to this generalization. Severe desquamation may now and then follow mild eruptions, and but slight scaling may develop after a well-marked exanthem.

When there has been no discoverable eruption there may be no desquamation, and even at times when there has been but a slight eruption present, the desquamation may be so insignificant as scarcely to be detectable.

Second Attacks of Scarlatina.—In the vast majority of individuals *one attack* of scarlet fever *will protect* against the disease *for life*. While there are many cases on record of second and a few of third and fourth attacks, it is quite obvious that in a disease which so often presents difficulties of diagnosis, the estimate of the number of cases reported must, to a certain extent, be discounted to allow for error. Willan never encountered an instance of second attack among 2000 cases of the disease that he attended. On the other hand, Trojanowsky estimated that 6 per cent. of his cases consisted of second attacks. Thomas, in an experience of many hundreds of cases, was able to convince himself of a second attack in only a single instance. Henoch, likewise, noted but a single instance of second attack. Kinnicutt saw two attacks within eight months in a boy five years of age.

¹ Pathogénie de la scarlatine, Paris, 1895.

Third attacks are of excessive rarity. Sir Gilbert Blane observed three attacks in a young lady "without the least suspicion of ambiguity or possibility of mistake in diagnosis." Richardson, Gillespie, Murchison, Bins, Moore, and Thompson have also recorded third attacks. Pritchard, of Glasgow, has reported the case of a patient who was treated in the same hospital for three attacks of scarlet fever occurring within two years.

Stiebel writes as follows: "In the case of a woman about fifty years of age, I have seen scarlet fever run its complete course four years in succession, the skin desquamating in certain areas in parchment-like pieces a half-shoe in length." Von Jürgensen, who quotes Stiebel, remarks, "From the latter circumstance I take the case to be a genuine one."

To our minds the regular periodicity of these attacks and the exfoliation of large sheets of epidermis point most strongly to the attacks having been of the nature of "erythema scarlatiniforme" of the exfoliative type, and not true scarlatina.

The same statement applies to the case reported by Jahn of a woman who had seven attacks, and to that of Henrici of a woman who is said to have had sixteen attacks of scarlet fever.

As showing the comparative frequency of multiple attacks of the infectious disease, the figures of Mycelius quoted by Sternberg are interesting:

	Second attacks.	Third attacks.	Fourth attacks.	Total.
Smallpox	505	9	0	514
Scarlet fever	29	4	0	33
Measles	36	1	0	37
Typhoid fever	202	5	1	208
Cholera	29	3	2	34

From this table it would appear that multiple attacks of scarlatina are less common than of the other exanthemata.

Körner,¹ who has made a careful study of scarlatina recurrences came to the conclusion that second attacks were rather more severe than first attacks. He mentions 8 cases in which the second attack was fatal. The first attacks commonly occurred in childhood before the age of ten, and the second attack from two to six years later, although in 6 cases a second attack occurred within a year.

Recurrent Eruptions and Relapses.—Considerable confusion has arisen in literature concerning the proper classification of secondary scarlatinal eruptions. It is well known that the exanthem of scarlet fever may, in rare instances, disappear and recur in a few days; it is manifestly improper to regard the reappearance of the eruption under such circumstances as a true relapse. Again, after complete convalescence from scarlatina the eruption of scarlatina and other symptoms may appear for a second time. It is somewhat difficult to set a definite time limit before which recurrences are to be regarded as relapses and after which they are to be looked upon as second attacks.

¹ Ueber Scharlach recidive. Jahrbuch für Kinderheilk., 1875 and 1876, N. F., ix.

Reasoning from analogy with the relapses of typhoid fever, we might regard as a *relapse* in scarlatina a redevelopment of several or all of the more important symptoms of the disease, occurring either during the course of the illness itself or immediately after the completion of convalescence. Cases recurring some time after convalescence has been established ought to be regarded as second attacks.

Relapses are, in all likelihood, due either to a reawakened activity of the scarlet-fever poison within the body, or to a reinfection from without. Kennan¹ believes that a patient with a mild scarlatina placed in a ward with severe cases might later be reinfected. From a study of the literature he thinks relapses are more common than formerly, and attributes the increase to the grouping of cases in special hospitals. True relapses usually occur during the second or third week of the disease.

In the majority of cases the recurrence is quite as complete in its symptomatology as the original attack. Not only does the eruption reappear, but there may be also renewed fever, vomiting, and sore throat. In other cases the first or the second attack may be rudimentary and poorly developed and may complement each other. The recurrence commonly runs a shorter and milder course and usually ends favorably; that this is not invariably so is instanced by the statistics of Körner, who noted a fatal termination in 8 cases of second attack.

Richardson gives an interesting account of a large number of relapses on board the frigate "Agamemnon." During an outbreak of scarlatina 300 out of 800 men were attacked. The ship was then thoroughly disinfected and aired for a month. Of 102 convalescents who returned to the ship, 18 developed relapses within five days. The disease, however, also recurred in many of those who remained on land. The second attacks were in some cases mild, but in others as severe as the original disease.

Relapses developing immediately after scarlatina, and second attacks within four or five weeks, have been reported by Bartels, Barthez and Rilliet, Faye, Gaupp, Jenner, Hillier, Kjellberg, Lefevre, Müller, Hall, Peacock, Richardson, Röbbelen, Schwarz, Smith, Solbrig, Steinbeck, Steinmetz, Steinhall, Stiebel, Trojanowsky, Wood, and others.²

Before accepting a secondary eruption as a true relapse, the possibility of its being a septic rash must be eliminated. These septic eruptions are often spotted in character, but may at times closely resemble the true eruption of scarlet fever. The roseolous eruption associated with protracted fever, referred to by Thomas as a pseudorelapse, is probably of this nature.

In very rare instances a *second relapse* may occur. Such a case has come under our observation, the temperature chart of which is reproduced (Fig. 70).

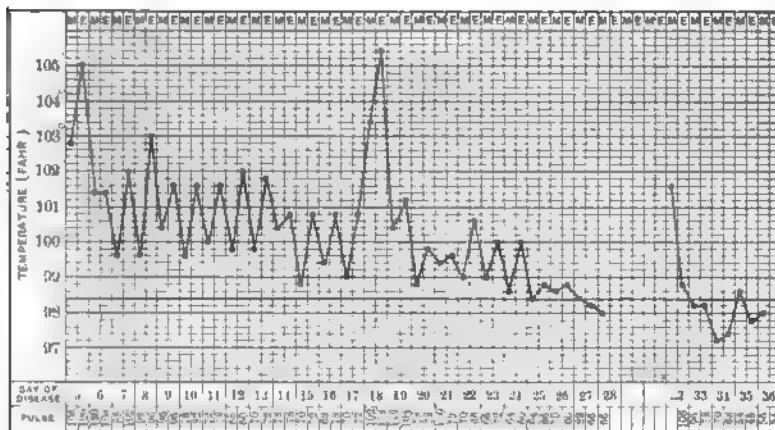
A. D., an Italian, aged twenty-one years, was admitted to the Municipal Hospital on June 9, 1892, on the fifth day of an attack of scarlet fever.

¹ Dublin Journal of Medical Sciences, 1898, No. 324.

² Quoted by Thomas, loc. cit., English translation, Ziemssen's Encyclopedia, p. 190.

He had a well-marked rash, sore throat, and high fever. The evening temperature on the day of admission was 105° F. On the ninth day there was well-pronounced desquamation. The temperature hovered between 99° and 101° F. until the eighteenth day, when it rose to 105° F. Accompanying this rise there were headache, abdominal pain and diarrhoea, and a recurrent, very bright rash; no throat symptoms. Urinary examinations were negative. Three days later a second desquamation began. The temperature now gradually declined, reaching normal on the twenty-seventh day of the disease. The patient was believed to be well, when on July 6th, or the thirty-second day of the disease, the temperature again rose to 101½° F. The patient complained of a slight sore throat, and a rash, followed by a fine desquamation, appeared on the face, arms, and trunk. The temperature declined quite promptly; the patient made a good recovery and was discharged from the hospital on July 26th.

FIG. 70



Scarlet fever, two relapses. A. D., aged twenty-one years.

It is seen that the first relapse occurred upon the eighteenth day of the disease, and the second upon the thirty-second, or just two weeks later.

Complications and Sequelæ of Scarlet Fever.

Throat.—Angina is an essential feature of the symptomatology of scarlet fever and cannot be regarded as a complication except where it is excessively developed. The most moderate expression of the scarlatinal sore throat is a uniform congestion of the uvula, anterior pillars, and tonsils. This form has been designated as *erythematous angina*. In more severe cases the mucous membrane is greatly swollen, and there is extension of the catarrhal inflammation posteriorly to the pharyngeal wall and anteriorly over the soft palate; these parts are of a deep-red color and bathed in a profuse mucoid secretion. The swelling of

the soft palate may be so intense as to seriously interfere with swallowing and to cause the regurgitation of liquids through the nose. The tonsils may also exhibit great increase in size and embarrass both deglutition and respiration.

In the *membranous* variety of angina the mucous membrane of the tonsils is covered with an exudate, which is usually of a yellowish or brownish tint and thinner and softer than the membrane of true diphtheria. While in most cases the pseudomembranous deposit is limited to the region of the tonsils, it is not uncommon for it to be present upon the half-arches and also scattered in patches upon the soft palate. It may likewise spread by way of the pharynx into the posterior nares and, in rare cases, to the tongue and buccal mucous membrane. Extension of the process along the Eustachian tube gives rise to inflammation of the middle ear, a most frequent complication of anginose scarlet fever. The glands about the angles of the jaw undergo inflammation and tumefaction and commonly suppurate. Pronounced constitutional symptoms accompany this variety of the disease. The temperature hovers about 104° or 105° F., and there is marked disturbance of the nervous system. Intense restlessness, delirium, stupor, coma, or convulsions may be present. The pulse is extremely frequent, often reaching 140 or 150 beats per minute. There is profound prostration, the urine contains albumin, and the patient is completely overwhelmed by the poison of the disease.

When there is extension of the process to the *nose* a purulent rhinitis is set up. There is a profuse discharge of a thin mucopurulent and often blood-stained material, frequently containing shreds of membrane. This irritating discharge inflames the nostrils and the upper lip and gives rise to impetiginous sores. The nose is swollen and the nostrils obstructed, causing considerable difficulty in breathing. An offensive odor is given off which can be detected some feet from the bedside. The nasal inflammation is attributed to the action of the streptococcus, the extension of whose pernicious activity may give rise to infection of the nasal sinuses.

French writers have called attention to the bad prognosis in these cases of early purulent coryza. The mortality in the Aubervilliers Hospital was over 50 per cent., and this complication was feared more than the most malignant forms of angina.

The membranous inflammation may extend to the *larynx* and produce serious difficulty in respiration. As has already been stated, however, laryngeal involvement is extremely rare in scarlet fever.

In normal scarlatina the larynx is exempted, and the mucous membrane, being in a healthy state, is not particularly susceptible to the noxious influence of the streptococcus or the diphtheria organism. In measles, on the other hand, the larynx is primarily involved and the soil is rendered favorable for the implantation of these micro-organisms.

The *gangrenous* variety of angina is fortunately rare, and is, for the most part, observed in hospitals. The gangrene may begin upon the tonsil, at the site of the rupture of an abscess. The necrotic process

may involve the entire tonsil, which sloughs out *en masse*. In some cases the gangrene is limited to the tonsillar tissues; in others it spreads beyond, attacking and destroying the palatine arches, the uvula, and a considerable portion of the soft palate. The affected parts are at first covered with a grayish-black, pultaceous deposit, which, when thrown off, discloses to view frightful loss of tissue. The odor emitted from these cases is foul and penetrating. The nose and ears are commonly involved and give exit to an ichorous discharge. The glands of the neck are greatly swollen; the constitutional depression is profound. In our experience the most common form of gangrenous angina has been characterized by circumscribed necrosis of the soft parts, particularly the soft palate, leading to irregular or rounded perforations about a half-inch in diameter. This condition may develop early, or may be postponed to the second or third week of the disease. We have observed this complication much more often in mixed cases of scarlet fever and diphtheria than in scarlet fever alone. The prognosis in this circumscribed gangrene is very unfavorable, although patients occasionally recover with considerable deformity of the soft palate.

In extremely rare cases gangrene may commit frightful ravages. The connective tissue of the neck may become involved, the overlying skin destroyed, and the muscles and large bloodvessels laid bare. Where the patient does not die of hemorrhage from erosion of the carotid artery, jugular vein, or other large bloodvessels, he is sure to succumb to the blighting influence of the septic poisoning. Recovery can only take place where the gangrene is limited to small areas.

Secondary Angina in Scarlet Fever.—The throat involvement thus far described occurs early in scarlatina and influences to a considerable degree the course that the disease takes.

A *secondary angina* may develop late in the disease; indeed, at times after convalescence is established. It is not rare for the tonsils to become the seat of a severe inflammation, increase greatly in size, and after a few days undergo suppuration. The neighboring soft palate becomes reddened and greatly tumefied. There is distressing pain, and speech and swallowing are difficult. We have here the usual symptoms of a suppurative tonsillitis or quinsy. In some cases the tonsillitis subsides without pus formation. We have observed these late anginas in hospital wards, a circumstance which suggests a second infection from without as the cause. Similar attacks of tonsillitis have occurred in ward maids and nurses, a fact which renders this view all the more plausible.

Postscarlatinal Diphtheria.—Before the days of bacteriology all cases of membranous angina were regarded as diphtheria. It is now recognized that the membranous deposit frequently seen in the throat early in the course of scarlatina is nearly always due to the streptococcus. Diphtheria is, as a rule, a complication of the stage of convalescence.

Caiger¹ gives the date of onset of 408 cases of postscarlatinal diphtheria:

¹ Article on Scarlet Fever in Allbutt's System of Medicine, p. 161.

TIME OF ONSET OF 408 CASES OF POSTSCARLATINAL DIPHTHERIA (CAIGER.)

Weeks.	Cases.	Percentage of total cases.
One	11	2.69
Two	36	8.82
Three	86	21.08
Four	77	18.87
Five	84	20.59
Six	46	11.27
Seven	25	6.13
Eight	27	6.61
Nine	18	4.41
Ten	13	3.18
Eleven	9	2.20
Twelve	9	2.20
Over twelve	15	3.67

It is seen from the above figures that the susceptibility to diphtheria is most pronounced from the third to the sixth week of scarlet fever.

Cases of postscarlatinal diphtheria are much more common in hospital than in private practice. In large hospital wards it doubtless occasionally happens that a secondary diphtheria remains undetected and exposes other patients to the infection. The mortality of mixed cases of scarlatina and diphtheria is, as would naturally be expected, higher than that of primary diphtheria.

There is nothing in the clinical or pathological picture of postscarlatinal diphtheria to distinguish it from primary diphtheria. It is usually limited to the tonsils and adjacent half-arches, although it may exhibit greater extent and spread to the posterior nares or to the larynx. The thick, grayish-white exudate contrasts strongly with the thin, smeary, yellowish or brownish deposit seen in the early stages of scarlatina. Paralysis, such as are seen after diphtheria, are excessively rare after scarlet fever. This observation is so well attested that when paralysis occurs after scarlatina there is a reasonable ground for the suspicion that a mixed infection has been present.

The diagnosis will, in large measure, rest upon the bacteriological findings. The presence of the Klebs-Loeffler bacillus in a throat which is the seat of exudate indicates the existence of diphtheria.

Since the specificity of the diphtheria bacillus has been established, numerous examinations of scarlatina throats have been made to determine the character of the membranous angina. Chabade,¹ of St. Petersburg, made cultures of 214 scarlatinal throats; of these, 98 had a catarrhal angina, 33 had a lacunar angina with a pseudomembrane in the tonsillar crypts, and 83 had a pseudomembranous angina involving the tonsils and adjacent soft tissues.

In the catarrhal group no diphtheria bacilli were found, but streptococci and, at times, staphylococci were present. In the lacunar anginas the Klebs-Loeffler bacillus was found twice. In the pseudomembranous cases the diphtheria organism was found eleven times, thrice almost in pure culture, and in eight cases associated with the streptococcus.

¹ De l'Association de la scarlatina avec la diphthérie, *La semaine méd.*, 1899, p. 184. Quoted by Northrup in von Jürgensen's article on Scarlatina in Nothnagel's *Encyclopedia of Practical Medicine*.

Variot and Devé¹ examined the throats of 525 cases of scarlatina. Of this number 62 had exudate in the throat, 30 of which proved to be true diphtheria.

Garret and Washbourn,² from cultures of the throat of 666 patients treated in the London Fever Hospital from 1896 to 1898, found that over 1 per cent. showed Klebs-Loeffler bacilli on admission.

For the past few years we have made cultures of all scarlatina patients admitted into the Municipal Hospital. The cultures were made at the home of the patient, in the ambulance, or after entrance to the ward.

In one series of cases, in which cultures were made after the admission of the patients to the ward, there were 167 negative results and 80 positive, or 32.35 per cent.

In a second series of over 500 cases, in which the cultures were taken either at the home of the patients or immediately after their reception into the ambulance, the results were as follows:

Negative cultures	.	.	74	Positive cultures	.	.	26
"	"	.	83	"	"	.	17
"	"	.	77	"	"	.	23
"	"	.	65	"	" (1 not recorded)	.	34
"	"	.	81	"	"	.	19
"	"	.	10	"	"	.	8
			<hr/> 390				<hr/> 122

Percentage, 28.8.

A further series of 500 cases, some cultured before admission to the wards and some shortly after, gave the following figures:

Negative cultures	.	.	87	Positive cultures	.	.	13
"	"	.	84	"	"	.	16
"	"	.	80	"	"	.	20
"	"	.	86	"	"	.	14
"	"	.	80	"	"	.	20
			<hr/> 417				<hr/> 83

Percentage, 19.9.

The aggregate of these figures gives a total of 1259 cases, of which 285, or 29.25 per cent., yielded positive cultures.³

The throats in many of the positive cases showed merely evidences of catarrhal angina. Subsequent cultures in the positive cases would at times be negative, but in not a small number of instances three or four positive cultures were obtained. There were comparatively few patients in whom the diagnosis of diphtheria would have been made from the clinical appearances.

The diphtheria patients are treated in a building which is quite apart from that occupied by scarlatina patients. Mixed cases are treated in the same building, but in a distant wing.

Ears.—Inflammation of the middle ear is, perhaps, the most common complication of scarlet fever.

¹ Soc. méd. des hôp., 1900, xvii. p. 1025; quoted by Northrup, loc. cit.

² Ann. de méd. et chir. enfant, 1899, t. iii.; quoted by Northrup, loc. cit.

³ These cultures were examined and reported upon by the City Bacteriological Laboratory, which is under the supervision of Prof. A. C. Abbott, of the University of Pennsylvania.

Its frequency varies with the character of the epidemic and with the age of the patient. In the anginose variety of scarlatina middle-ear disease follows in almost every case. Some epidemics appear to be characterized by a much smaller incidence of ear complications than others. Holt mentions the fact that in an epidemic occurring in the New York Infant Asylum in the spring and summer of 1889, there were 73 cases of scarlet fever and not one developed otitis. In a fall and winter epidemic in the same institution, two years later, of 43 cases of scarlet fever, 20 per cent. developed otitis. The frequency of otitis in different epidemics is influenced by the degree of angina present, and also to some extent by season, middle-ear trouble being more prevalent in the colder months. Infants are more liable to develop otitis media than children of more advanced years. This may be due to the relatively large size of the Eustachian tube in infancy.

Finlayson states that otitis was present in 10 per cent. of 4397 cases of scarlet fever reported by him. Caiger¹ analyzed 4015 cases of scarlatina, and determined that otitis media with discharge took place in 11.05 per cent. thereof. Burckhart reports this complication in 33 per cent. of cases. In attacks with severe throat involvement otitis occurs, according to Holt, in fully 75 per cent. of cases.

Bader and Guinon² report 33 per cent. involvement in the form of mild or catarrhal otitis, and purulent otitis in but 4.5 per cent. of cases of scarlatina.

Middle-ear disease results from direct extension of inflammation from the nasopharynx and doubtless through the action of the bacteria, chiefly the streptococcus. This complication may develop at any time during the course of scarlet fever, even as late as during convalescence. It is apt to develop early in bad cases with severe throat involvement. In 18 cases of otitis media recently observed by us the discharge appeared upon the following days:

DAY OF SCARLET-FEVER ILLNESS UPON WHICH EIGHTEEN CASES OF
OTITIS MEDIA DEVELOPED.

1 on the 6th day	1 on the 19th day.
1 " " 8th "	2 " " 19th "
2 " " 9th "	1 " " 20th "
1 " " 10th "	1 " " 21st "
1 " " 11th "	1 " " 22d "
1 " " 13th "	1 " " 23d "
1 " " 16th "	1 " " 33d "
1 " " 17th "	1 " " 35th "

One or both ears may be affected; when both are attacked the discharge does not, as a rule, appear simultaneously, an interval of four or five days or a week separating the two attacks.

When the ear complication develops early in the course of the disease, while the temperature is high and nervous manifestations still present, the symptoms thereof are apt to be obscured by the general condition of the patient. When the otitis appears at a later date, after the scar-

¹ Scarlet Fever, Allbutt's System of Medicine, New York, 1897, vol. III. p. 150.

² See Moizard, Scarlatine, in *Traité des mal. de l'enfance*, Paris, 1897, vol. I.

latinal fever has declined, its development is accompanied by a sharp rise of temperature. The fever is usually preceded by pain, although this symptom is extremely variable.

Infants will often carry their hands to their ears and utter sharp shrieks. In some cases there is enlargement and tenderness of lymphatic glands about the ear. The otitis may be a simple *catarrhal* inflammation, or it may be *purulent or suppurative*. In the former variety the duration of the affection is much shorter and of a less serious character. The fever, pain, and tenderness subside rapidly after spontaneous rupture or incision of the tympanic membrane.

Purulent otitis media pursues a much more protracted course. A mucopurulent discharge may continue for weeks or, indeed, the condition may lapse into a chronic suppurative otitis. The immediate dangers associated with this condition are extension of the purulent inflammation to the mastoid cells or meninges of the brain, the erosion of bloodvessels, with the production of serious hemorrhages, and finally the development of septicæmia or pyæmia.

Cases are on record in which the *erosion of large bloodvessels* has led to fatal hemorrhage. Baader¹ reports the case of a three-year-old boy suffering from a purulent otitis complicating scarlatina, who developed on the eleventh day of the disease a severe and uncontrollable hemorrhage from the ear which caused death on the third day. Autopsy disclosed a perforation of the posterior wall of the tympanic cavity and an erosion of the lateral sinus.

Hessler² records a case in which a fatal hemorrhage resulted from ulceration of the carotid artery.

A similar case is reported by Hynes,³ in which a sudden and unlooked-for hemorrhage poured from the right ear in a four-year-old child. The child later vomited blood in large quantities and died. It was thought that the bleeding came from the internal carotid artery.

Hüber⁴ reports a case of hemorrhage from an eroded vessel which caused a hæmatoma of the neck, the opening of which resulted fatally. Kennedy has reported three fatal cases of hemorrhage, and Möller and West each one instance.

The following case of *septicæmia* associated with purulent otitis was observed by us in the Municipal Hospital in 1889:

F. F., a boy aged thirteen years, was admitted to the hospital on February 2d, with a bad anginose scarlet fever. His condition improved for a week, the temperature reaching normal. On February 10th the patient had a chill with a rise of temperature to $104\frac{3}{5}^{\circ}$ F. On the following day another chill and a temperature of $107\frac{2}{5}^{\circ}$ F. The next day the temperature rose to $107\frac{4}{5}^{\circ}$ F. For a period of ten days there occurred the most violent rises and falls of temperature, the extreme limits being $95\frac{4}{5}^{\circ}$ and $107\frac{4}{5}^{\circ}$ F., an excursion of 12 degrees. Chills recurred each day and on one occasion repeated vomiting. The ear which was discharging

¹ Acute Verblutung bei Scharlach, Corres. bl. f. Schweiz. Aerzte, 1875, Bd. v.

² Quoted by Forchheimer, loc. cit.

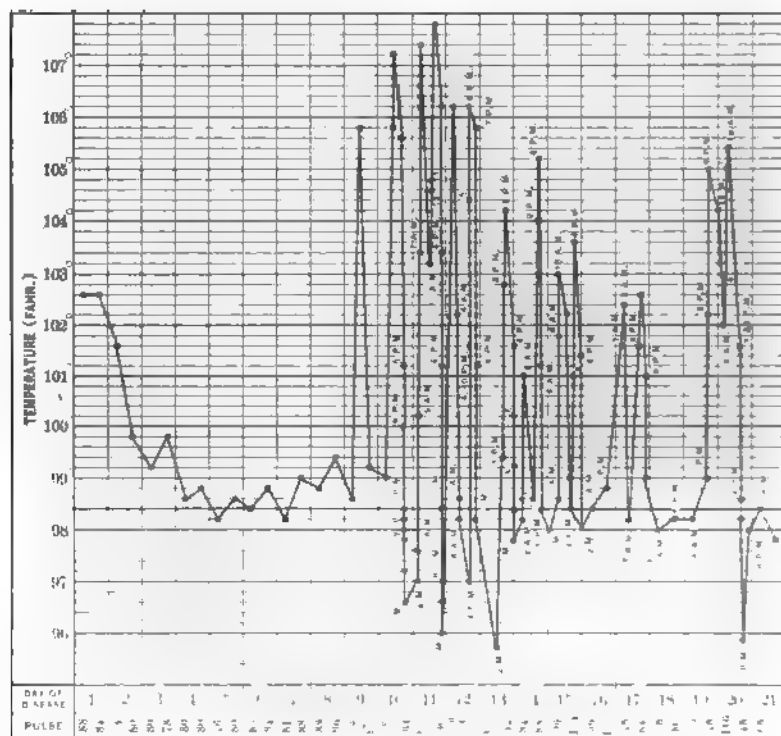
³ Quoted by Forchheimer, loc. cit.

⁴ Deutsche Archiv f. klin. Med., Bd. viii. p. 422.

was kept thoroughly clean with a carbolized solution. By February 27th the patient had recovered sufficiently to leave his bed (Fig. 71).

The immediate dangers of purulent otitis having been passed, there remain severe structural changes which may seriously interfere with the sense of hearing. There may be partial or complete loss of the tympanic membrane upon one or both sides; occasionally the ossicles are destroyed and thrown off. Ulceration and necrosis of the walls of the tympanum may occur, with the development of further complications to which

FIG. 71



Remarkable excursions of temperature due to suppurating otitis media. F F, aged thirteen years, admitted to hospital in critical condition—bad throat and mouth; ears discharging on second day of disease. Various rises of temperature accompanied by chills, ultimate recovery.

reference will be made later. The *labyrinth* may be attacked in rare cases. Pye, Phillips,¹ and others have reported cases in which labyrinthine structures were necrosed and discharged *en masse*. These patients were, of course, left completely deaf. Bezold² gives the results of 185 cases of scarlatinal otitis: "In 30 there was entire destruction of the membrana tympani, with the loss of one or more bones; in 59 the perforation comprised two-thirds or more of the membrane; in 13 there were smaller perforations; in 44 there were granulations or polypi; in

¹ Quoted by Holt, *loc. cit.*

² Quoted by Holt, *loc. cit.*

15 there was total loss of hearing on one side, and in 6 of the cases on both sides; in 77 of the cases the hearing distance for low voice was less than twenty inches."

Burckhardt-Merian¹ reported 85 cases of ear complications of which 72, or 84.7 per cent., involved both ears. Of 4309 cases of acquired deafness and dumbness, 445, or 10.3 per cent., were due to scarlet fever. May, of New York, has collected similar statistics; of 5613 cases of deaf-mutism, 572 were traceable to attacks of scarlet fever.

Purulent otitis may, in rare cases, give rise to disease of the *mastoid antrum*. This may occur during convalescence from scarlet fever or may develop after the otitis has become chronic. The mastoid region is painful and tender and acquires a characteristic appearance—the great postauricular swelling causing the ear to stand out prominently from the head. The temperature rises to 103° or 104° F., and, unless there is operative interference, brain symptoms may manifest themselves. On incision a mastoid abscess is found present. At times a superficial abscess is found in the region of the mastoid, without actual involvement of the mastoid cells.

Thrombosis of Lateral Sinus.—Thrombosis of the lateral sinus is occasionally encountered in cases in which cerebral abscess or meningitis subsequently develops. The onset is sudden, with chills and high and irregular fever.

Facial Palsy.—Facial palsy is by no means a rare complication of scarlatinal otitis. We have observed this paralysis in a number of cases of severe middle-ear disease. It is due to an extension of inflammation from the tympanum to the facial nerve, where it passes through the roof of the cavity. The symptoms do not differ essentially from facial palsy occurring from other causes.

Abscess of the Brain.—Abscess of the brain may result from extension of the suppurative inflammation from the middle ear. The petrosquamous suture being patulous in children, an avenue of infection to intracranial structures is readily offered. The periosteum of the tympanum is continuous with the dura mater, and extension of inflammation may occur along this membrane. In addition, the infection may be carried to the brain through the medium of the veins.

Purulent Meningitis.—Purulent meningitis is an extremely serious complication that may arise from a suppurative otitis. It may have its origin in thrombosis of the lateral sinus or may develop from necrosis of the roof of the tympanic cavity. There are usually high fever, stiffness of the neck, retraction of the head, vomiting, and, at times, paralytic eye symptoms. Death occurs ordinarily in about a week. The following case will illustrate the symptomatology of this complication:

W. J., aged three years, was admitted to the Municipal Hospital on April 9, 1903, with a severe attack of scarlet fever. On the sixth day of the disease the right ear discharged. Fever was protracted, the temperature not touching normal until the thirtieth day. Later the

¹ Ueber den Scharlach in seinen Beziehungen zum Gehörorgan; Volkmann's Sammlung klin. Vorträge Chir., No. 54.

temperature rose as the result of a cervical abscess. There was no fever from the forty-fourth to the fifty-fourth day. At this time the temperature began to rise and the patient vomited. He cried out sharply upon being disturbed. A gradually increasing stuporous state developed. The neck was rigid and the head retracted. The pupils were equal and reacted to light. The patient gradually lapsed into complete coma. The temperature rose to $106\frac{3}{8}^{\circ}$ F. and the patient died on the ninth day of the complication and the sixty-fourth day of the scarlet fever. When the skull was opened at autopsy a foul odor was immediately noticed. A purulent exudate was found covering the entire base of the brain, but involving chiefly the left side. The pia mater under the left cerebellum was infiltrated with pus, and there was free pus in the various fossæ. There was no discoverable caries of the petrous portion of the temporal bones, and on opening these no pus could be detected. Cultures from the purulent material demonstrated the presence of the *staphylococcus pyogenes aureus*.

Complete Deafness.—Complete deafness not due to middle ear disease occurred in a boy, aged five years, at the Municipal Hospital, during convalescence from a well-marked attack of scarlet fever. The patient had been out of bed for a number of days, when he was suddenly taken ill with high fever, vomiting, heavily coated tongue, and delirium. This was shortly followed by pronounced mental hebetude; vomiting persisted for several days, nothing being retained upon the stomach. Mental dulness continued for several days, after which, upon the clearing up of the mental faculties, it was noticed that the patient was absolutely deaf. There had not been any discharge from the ears nor any other evidence of otitis. The mastoid region was normal. The temperature for a week or ten days was markedly irregular, fluctuating rapidly between 99° and 104° F. About the same time that deafness was noted there was a paralytic strabismus. The patient left the hospital absolutely deaf. The internal ear was doubtless diseased in this case, perhaps as the result of a localized meningitis.

Eyes.—In cases of severe scarlet fever, particularly where there is a purulent rhinitis, extension of the inflammation may take place and a severe conjunctivitis set up. More often the conjunctivitis that develops is of a mild character, with injection of the bloodvessels of the sclera and lids, increased lacrymation and photophobia.

The *lacrymal duct* and *gland* may become involved through the infection that has its origin in a purulent coryza. Through this channel other ocular structures may subsequently be attacked.

Primary Keratitis.—Primary keratitis with its unfortunate train of symptoms develops at times, particularly in scrofulous subjects. We recall a corneal ulcer in a colored child, who had previously suffered from keratitis, in whom perforation with prolapse of the iris occurred. Leichtenstern reports 2 cases of corneal ulcer and 1 of hypopyon keratitis occurring in a severe epidemic in the hospital at Cologne. Thomas quotes Schröter as saying that the cornea may be affected primarily and independently, usually in the way of rapidly progressing abscesses

or suppurating ulcers or pernicious keratomalacia, in which the cornea of one or both eyes, without any marked symptoms, becomes turbid in a few days, is transformed in its totality into a turbid, dirty, grayish-white membrane, and exfoliates piecemeal. The inflammatory process may travel thence over the uveal tract and cause a panophthalmitis.

Choroiditis.—Choroiditis may, in rare cases, complicate scarlet fever. In the epidemic already alluded to Leichtenstern saw a case of choroiditis which ended in phthisis bulbi.

In those cases in which a severe nephritis is present ophthalmoscopic examination may reveal the existence of an *albuminuric retinitis*. Both eyes are usually equally and simultaneously affected. After a protracted course more or less complete restoration usually results.

Temporary blindness, or *amblyopia*, may complicate the kidney condition; after some days complete vision is usually restored. We have personally observed such cases. Porter¹ saw a young girl with severe complications, develop temporary blindness with exophthalmos from infiltration of the cellular tissue of the orbit. Duval² saw a similar case of exophthalmos lasting ten days, the sight being subsequently fully restored.

Within the past few years we have observed in the Municipal Hospital two cases of *orbital cellulitis* complicating scarlet fever and leading to a fatal termination. These cases were seen and studied by Dr. Burton K. Chance,³ Assistant Surgeon to the Wills Eye Hospital, Philadelphia, to whom we are indebted for careful notes of the cases:

Case I. was a boy, aged seventeen years, who during a protracted convalescence from a severe scarlet fever developed a sudden diffuse cellulitis of the right orbit. A chill and sharp rise of temperature were followed by an effusion of fluid into the areolar tissue, with protrusion of the globe. The eyelids were red and excessively oedematous. The fundus was at first pale, but later intensely red, with fine hemorrhages. There was marked swelling of the disk, an overdistention of the veins, and contraction of the arteries. A day or two before death the cornea became necrotic and the eye was lost. High fever, delirium, and coma preceded death, which took place one week after the development of the complication. The examination of the orbital structures after death revealed only a diffuse serous infiltration; there was no evidence of intraocular suppuration.

Case II. was a boy, aged ten years, who was convalescing from scarlet fever, when there developed in the right orbit an acute congestion with infiltration of the tissues, producing proptosis between the intensely oedematous lids. The local symptoms were similar to those in the first case. Throughout the course of the process the cornea remained unaffected. Deep incisions were made into the periocular tissues, evacuating a quantity of blood-tinged serum, but no pus. On the eighth

¹ Quoted by Thomas.

² Quoted by Thomas.

³ Dr. Chance reported his findings in a paper read before the Philadelphia County Medical Society, May 27, 1903. This was published in *American Medicine*, June 13, 1903, p. 960.

day after the onset of the complication the patient was seized with convulsions and died. Permission to make an autopsy was refused.

In rare cases failure of vision may be due to atrophy of the optic nerve or to detachment of the retina. *Optic neuritis* may occur with meningitis or without such involvement, as in a case reported by Putnam.

Heart.—The heart may suffer in scarlet fever from (1) the scarlatinal toxin, (2) as a result of nephritis, and (3) from secondary infections, such as rheumatism, pyæmia, etc.

That the scarlatinal poison has a direct influence upon the heart is seen in the early tachycardia, the heart beats being out of all proportion to the temperature. Furthermore, in malignant cases that are overwhelmed at the onset by the poison of the disease, the symptoms are those of an acute cardiac failure; the pulse is rapid, small, and irregular; the extremities are cold, and pallor and cyanosis are often present. In severe cases of the disease, the scarlatinal toxin, according to Romberg,¹ may early cause a pronounced *dilatation of the heart*.

The occurrence of nephritis in scarlet fever naturally leads to changes in the cardiac muscle. Whenever the kidney involvement is at all pronounced there will be found a *hypertrophy and dilatation of the heart*. The changes are apt to be present upon both sides, but the preponderant enlargement is nearly always found upon the left side.

Riegel² states that in most, if not in all, cases of scarlatinal nephritis there is an increased arterial tension from the very beginning. After the blood pressure has persisted for some time, the heart enlarges as a consequence. In some cases the increased size of the heart may be noticed a few days after the onset of the nephritis. It is readily seen how this form of cardiac disease is produced. The development of nephritis by raising the arterial tension throws an extra burden upon the heart; if the heart has already been injured by the influence of the scarlatinal poison, the strain may be too much and acute dilatation may result. If the heart muscle has more recuperative power a compensatory hypertrophy may take place.

If the left heart develops a pronounced insufficiency, a dilatation of the right side will usually occur. When this results we see the usual symptoms of cardiac insufficiency—dyspnoea, rapid pulse, enlargement of the liver, etc. A murmur may or may not be heard over the mitral orifice. It is important to recognize the fact that the bruit is not due to an endocarditis, but to cardiac dilatation. This murmur will be found to disappear as the heart improves.

Myocarditis.—Myocarditis is the heart condition which is most frequently called into existence by the scarlatinal toxin and by the associated nephritis. The other forms of heart disease are more commonly associated with secondary rheumatism or septic infection. Ashby found *endocarditis* not uncommon with rheumatoid affections

¹ Ueber die Erkrankungen des Herzmuskels bei Typhus Abdominalis, Scharlach, etc., Deutsch. Archiv f. klin. Med., Bd. xlviii, p. 369, and Bd. xlix p. 413.

² Ueber die Veränderungen des Herzens, etc. bei Acuter Nephritis, Zeitschr. f. klin. Med., 1884, Bd. vii, p. 280; quoted by von Jürgensen, loc. cit.

developing in the third or fourth week of scarlet fever, but not with the early synovitis.

Roger¹ has found endocarditis an uncommon complication. Out of 2213 cases of scarlet fever (1727 in adults) examined by him, he saw but 2 cases of endocarditis. On the other hand, he noted extracardial murmurs 692 times.

McCollom,² in an analysis of 1000 cases of scarlet fever, says: "A mitral systolic murmur was detected in 187 cases; *bruit de galop* in 5 cases; irregular action of the heart in 54 cases; endocarditis in 3 and pericarditis in 5 cases." Many of the murmurs referred to were thought to be due to lack of tonicity of the heart muscle as a result of the action of the scarlatinal poison.

Von Jürgensen expresses the opinion that endocarditis of the cardiac wall is more common in scarlet fever than valvular involvement. He further believes that this mural endocarditis may slowly extend to the valves after the attack of scarlet fever is over.

Pericarditis.—Pericarditis occurs from time to time in the course of scarlet fever, being much more common in association with nephritis, synovitis, and pyæmia than with cases of simple scarlatina. Roger has observed cases of dry pericarditis, both at the height of the disease and during convalescence.

In pyæmia endocarditis and pericarditis are commonly present; the exudate in the latter affection in such cases may be purulent. Roger saw a child, aged eight years, with a severe scarlet fever complicated by a purulent otitis media, die on the forty-seventh day of the disease. At autopsy the pericardium was covered with a false membrane; there was an ulcerative endocarditis and an abscess in the wall of the left ventricle. The streptococcus was recovered from these lesions.

In our own experience severe cases of endocarditis have been rare, and, when present, have been accompanied by joint involvement. We recall a twelve-year-old boy who during the third week of scarlet fever had articular swellings which recurred from time to time for several weeks. He also had a well-marked albuminuria. This patient developed at a later period an endocarditis which severely damaged the mitral valve; he subsequently exhibited a presystolic murmur with a pronounced thrill over the mitral region. The murmur had a peculiar crowing sound of a musical character. After undue exertion he developed a sudden dilatation of the heart with rapid pulse and a change in the character of the murmur which now became blowing. He was tided over this crisis, but a few weeks later he again developed a cardiac dilatation and died. A rather unusual symptom in this patient was a *geographic erythema* which appeared over the trunk from time to time, recurring apparently with fresh joint involvement and then gradually fading away.

In another fatal case we observed a vegetative endocarditis attacking the mitral and aortic valves, associated with pleurisy, joint swellings, and extensive purpura.

¹ Loc. cit., p. 941.

² Scarlatina, Medical and Surgical Reports, Boston City Hospital, 1899.

Lymphatic Glands.—A generalized enlargement of the lymph glands constitutes a part of the normal symptomatology of scarlet fever. The subcutaneous lymph nodes in all parts of the body undergo some hyperplasia, but those situated in the neighborhood of the facial orifices undergo the greatest tumefaction. That this *primary* lymphatic involvement is due to the scarlatinal toxin is evidenced by the fact that the lymphoid elements of the spleen, liver, and intestines become likewise hyperplastic.

It is only when the lymph glands become excessively enlarged or undergo suppuration that a complication is added that augments the danger of the disease.

The most aggravated cases of lymphadenitis occur in association with the anginose variety of scarlet fever.

FIG. 72



(greatly swollen and suppurating maxillary glands.

In these cases the glands at the angle of the jaw undergo rapid enlargement, causing the head to be thrown backward. This complication increases the suffering and danger of the child, who by this time is already prostrated by the poison from a sloughy throat and discharging ears and nose. The temperature is high, the nervous system markedly disturbed, and death imminent.

By the fifth or sixth day of the disease the maxillary glands may already have attained the size of small apples. They are hard at first, but gradually break down and suppurate.

In cases of scarlet fever of less severity, but accompanied by pronounced angina, it is not at all rare for the glands at the angle of the

jaw to enlarge and suppurate. In cases terminating favorably the gland after incision becomes gradually drained of pus in the course of a few weeks and heals up. One or both glands may suppurate, the process being simultaneously bilateral in the bad cases. It is rare for any other glands to undergo suppuration early in the course of the disease, save in the malignant cases presently to be described.

The connective tissue of the neck may, in large part, become the seat of a *diffuse cellulitis* which develops during the first or second week in connection with great glandular intumescence in severe cases. This frightful condition, known as Ludwig's angina (*Angina Ludovici*), is fortunately rare, for it is almost inevitably fatal. The neck is diffusely swollen, often from the clavicles to the chin and parotid region; instead of the natural concavity of this region the induration makes of the curve a straight line.

The head is forced back by this extensive brawny infiltration. The neck is hard, indeed often board-like to the touch, and of a bluish-red color. There may be great difficulty in breathing, owing to the unnatural position of the head and pressure upon the larynx. The constitutional symptoms accompanying this condition are those of a profound septicæmia; the fever is high and irregular, and often associated with chills and sweats. The pulse is rapid and feeble, and the prostration great. Death may occur before suppuration of the infiltration takes place. In other cases suppuration occurs, with extensive destruction of tissue. A fatal result may occur from pressure upon the air passages or from œdema of the glottis. In other cases extensive burrowing of pus may take place, the purulent fluid finding its way into the thorax, as in the cases reported by Hensch and Bartels. Cremen¹ saw the pharynx perforated, the food coming out through the opening.

One of the most dangerous consequences of the extensive suppuration is erosion of the large veins of the neck. Baader reports two cases of fatal hemorrhages after extensive suppurating cellulitis. The first occurred in a four-year-old boy, during the fourth week of a scarlet fever complicated by pharyngeal diphtheria. A huge swelling extended from the jaw-bone to the larynx on the left side. This was incised to relieve suffocative symptoms. Instead of pus blood clots were removed, after which a thick stream of arterial blood issued forth, which was checked by compression. Four days later a fatal hemorrhage occurred from the nose and mouth. The autopsy showed that the external carotid artery had been destroyed by gangrene.

In the second case, a six-year-old child developed Ludwig's angina on the thirteenth day of scarlet fever. This was incised below the clavicle; profuse hemorrhage later occurred from this wound. Autopsy showed a large opening in the external jugular vein, where it had been eroded by the suppurative process.

A form of *late glandular involvement* is not uncommon in the course of scarlet fever. This takes place after the fever and acute symptoms

¹ Quoted by Thomas.

have subsided, not infrequently occurring during convalescence. The glands at the angle of the jaw and the submaxillary lymphatic gland are those usually affected. There is moderate enlargement of the gland, which becomes quite hard and somewhat tender. Suppuration may occur, but more commonly the gland gradually decreases in size and resumes its normal dimensions.

Retropharyngeal Abscess.—Retropharyngeal abscess may occur as the result of the burrowing of pus from suppurating glands. Bokai¹ observed this complication seven times in 664 cases of scarlet fever in children. In 6 of these cases the abscess was attributed to an adenitis of the retropharyngeal glands. In a fatal case this complication was seen as early as the fifth day of the disease.

Kidneys.—No exanthematous disease is so frequently complicated by inflammation of the kidneys as scarlet fever. It is rare for a severe attack of this disease to run its course without the development of albuminuria. The frequency of renal complications varies very greatly in different epidemics; at one time albuminuria with dropsy is a striking feature of the prevailing type of the disease, while in other epidemics it is rare to observe this complication. In general terms it may be stated that severe epidemics of scarlatina are more apt to be accompanied by nephritis than the mild ones.

Divergent opinions have been expressed from time to time as to the cause of the scarlatinal nephritis. Steiner claimed that nephritis was a part of the symptomatology of the disease, just as much, indeed, as the rash was. Most writers, while not subscribing to so radical an opinion, regard the kidney involvement as due to the scarlatinal poison, whatever that may be. The great frequency of this complication in scarlet fever and certain peculiarities in the clinical picture have led some writers to regard the nephritis as a specific entity peculiar to this disease. It is true that the clinical course presents features which, to a certain extent, differentiate nephritis in scarlet fever from this affection occurring under other circumstances. The great tendency to anasarca, which is particularly evident in certain epidemics, the onset of the complication at a rather uniform period, and the favorable outcome in cases presenting most alarming symptoms, give to scarlatinal nephritis a rather characteristic clinical picture. Moreover, the pathological changes are of a quite uniform character, the essential condition being an acute glomerulonephritis.

Forchheimer pertinently remarks, however, that almost identical changes may be produced in the kidney by the administration of toxic doses of cantharidin. It must also be remembered that many acute infectious diseases are complicated by the development of nephritis, and this is particularly true of those maladies in which we have a secondary infection with streptococci; for instance, in smallpox. In a careful analysis of the urine of 128 cases of smallpox, we found albuminuria in 65 per cent. and tube casts in 45 per cent. of the cases. How

¹ *Jahrbuch f. Kinderheilk.*, N. F., Bd. x. p. 106; quoted by von Jürgensen, loc. cit.

far the streptococcus may be held accountable for the inflammation of the kidneys in scarlatina is a matter difficult to solve. Most writers concede to this cause a certain percentage of the renal complications. The finding of streptococci in the kidneys at autopsy does not of necessity convict these micro-organisms of producing the nephritis. With the discovery of the *causa causans* of scarlet fever there will doubtless come a more satisfying elucidation of the etiology of the associated nephritis.

Albuminuria may appear *early* in the course of scarlatina; that is, during the first week of the disease. This albuminuria is usually *transient*, not lasting more than one or possibly two days. It, moreover, seldom gives rise to any definite symptoms. Inasmuch as it is usually coincident with high fever, it is regarded as a *febrile albuminuria*.

It should be remembered, however, that this albuminuria is not merely functional, but is due to an acute degeneration of the tubules of the kidney, the result, doubtless, of the elimination of toxins.

Some authors refer to an early suppression of the urine; when this occurs it is nearly always a manifestation of severe nervous disturbance.

The nephritis that occurs early does not, as a rule, give rise to uræmic symptoms, nor does it lead of itself to a fatal termination. In severe cases of scarlet fever that terminate early in death, structural alterations may be found in the kidneys, in common with the changes in the liver, spleen, heart, and other organs.

Postscarlatinal Nephritis, or Nephritis of Convalescence.—It is after the subsidence of the acute symptoms that the true scarlatinal nephritis is prone to develop. Most of the cases will be found to begin during the third week of the disease. We have seen albuminuria appear for the first time as late as the sixty-third day, and it may even develop at a later period.

Below is appended a series of 61 cases of albuminuria recently observed among 150 cases of scarlet fever:

ALBUMINURIA IN SCARLET FEVER; DAY UPON WHICH SIXTY-ONE CASES OF ALBUMINURIA WERE FIRST NOTICED.

First Case noticed.		First Case noticed.	
1. 3d day.	Transient.	32. 17th day	Lasted twenty-three days.
2. 4th "	"	33. 17th "	Lasted four days.
3. 4th "	"	34. 17th "	Transient.
4. 5th "	"	35. 19th "	Lasted nine days.
5. 6th "	"	36. 19th "	Lasted twenty-one days.
6. 6th "	"	37. 19th "	Transient.
7. 7th "	"	38. 19th "	Persisted.
8. 7th "	"	39. 20th "	Transient.
9. 7th "	"	40. 20th "	Lasted eighteen days.
10. 8th "	"	41. 21st "	Transient.
11. 8th "	"	42. 21st "	"
12. 8th "	"	43. 21st "	Lasted seventeen days.
13. 8th "	"	44. 22d "	Transient.
14. 9th "	"	45. 22d "	"
15. 10th "	"	46. 23d "	"
16. 10th "	"	47. 23d "	"
17. 10th "	"	48. 23d "	Lasted seventeen days.
18. 10th "	"	49. 23th "	Persisted.
19. 11th "	"	50. 24th "	Transient.
20. 11th "	"	51. 24th "	"
21. 12th "	"	52. 29th "	"
22. 12th "	Lasted eight days.	53. 32d "	"
23. 12th "	Transient.	54. 33d "	"
24. 14th "	"	55. 34th "	"
25. 14th "	"	56. 36th "	"
26. 14th "	"	57. 36th "	"
27. 14th "	"	58. 37th "	Lasted six days.
28. 14th "	At intervals until fifty-sixth day.	59. 39th "	Transient.
29. 15th "	Lasted ten days.	60. 41st "	"
30. 16th "	Lasted fifteen days.	61. 63d "	Lasted six days.
31. 17th "	Transient.		

It will be seen upon reference to the above table that almost all of the cases of albuminuria observed during the first two weeks of the disease were transient, lasting but a day or two. In many of the early cases but a trace of albumin was found. None of the patients in this series had anasarca or any severe uræmic symptoms. It is proper to add that these cases occurred at a time when the type of scarlet fever was quite mild.

As has already been stated, the frequency of nephritis varies strikingly in different epidemics. Roger gives an interesting analysis of the occurrence of albuminuria in 2157 cases of scarlet fever in adults and children.

	Men.	Women.	Children.
Number of patients	718	1009	430
Fatal cases (with albuminuria)	16	23	14
Patients cured (having had albuminuria)	264	308	91
Total number of cases of albuminuria	880	331	105
Frequency of albuminuria per 100 patients	38.9	33.1	24.3
" " " 100 cured	37.6	31.2	21.8

It will be seen from these figures that albuminuria is less frequent in children than in adults.

Vogl reports as high an incidence of nephritis in one epidemic as 34 per cent. Cadet de Gassicourt has observed late nephritis in 30 per

cent. of all cases. It was present in 18 per cent. in a series of cases studied by Friedländer. Baginsky has recently reported 88 cases of nephritis among 919 cases of scarlet fever (a percentage of 9.57) observed in the hospital during a period of five years.

Ashby states that the average of several years in hospital cases under his observation was 6 per cent. In a series of 2078 cases Caiger reports acute nephritis in only 3.32 per cent. The wide discrepancy in these figures may be due, to some extent, to the standards adopted in interpreting the presence of nephritis, but wide variations are not uncommon in different epidemics. Holt states that the average is from 6 to 10 per cent.

AGE.—Hetzka, of St. Petersburg, has compiled statistics of 138 cases of nephritis occurring in children in the Elizabeth Hospital; these figures indicate that children under two years of age are very much less apt to develop nephritis than those above the age of two or three.

				Nephritis.			
Under 1 year	.	.	25 cases.	1 case	.	.	4 per ct.
Between 1 and 2 years	.	.	107 "	5 cases	.	.	4.6 "
" 2 " 3 "	.	.	106 "	12 "	.	.	11.3 "
" 3 " 4 "	.	.	79 "	16 "	.	.	20.2 "
" 4 " 5 "	.	.	80 "	20 "	.	.	23.2 "
" 5 " 6 "	.	.	89 "	18 "	.	.	21.9 "
After 6 "	.	.	300 "	60 "	.	.	16.6 "

While severe cases of scarlet fever are more apt to be followed by nephritis than mild cases, it is impossible in any individual instance to prophesy the development or the non-occurrence of this complication, because the scarlatinal attack may be severe or mild. There appears to be something in the individual make-up which predisposes one toward or protects one against a complicating nephritis. Doubtless each individual has certain organs or tissues which are more vulnerable to the noxious influence of the scarlatinal poison than others.

The opinion formerly held, that "catching cold" plays any important role in the etiology of nephritis complicating scarlatina, is being discredited by most writers on the subject.

SYMPTOMS OF NEPHRITIS.—In some patients albumin appears in the urine for the first time during convalescence; in other cases albuminuria is a reawakening of the nephritic process that manifested itself early during the acute stage of the disease.

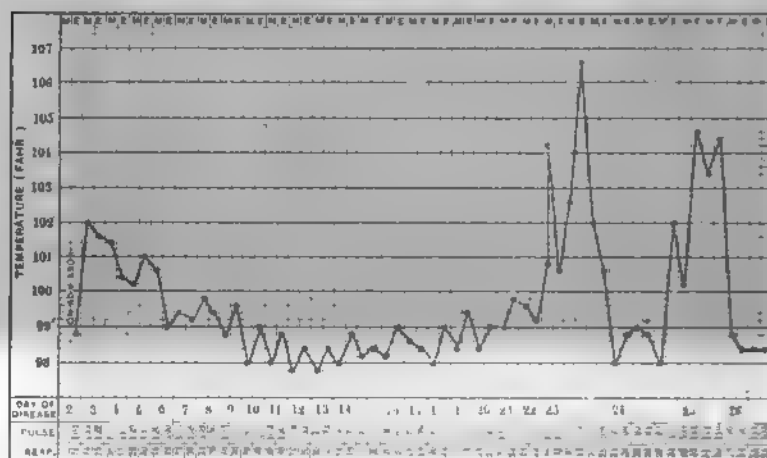
The nephritis with its accompanying symptoms of intoxication ordinarily comes on insidiously, although in some instances it may explode with alarming suddenness. The development of albuminuria is accompanied, or often preceded, by a rise of temperature. A febrile elevation in the third week of scarlet fever will commonly be found to be due to nephritis. The character and duration of the fever are extremely variable. It may persist for a number of days or may drop to normal at the end of forty-eight or seventy-two hours. The temperature often exhibits striking irregularities, dropping to normal and suddenly rising again. Ordinarily the pyrexia is moderate in intensity, but it may rise to great height. We have seen a temperature of $106\frac{3}{5}^{\circ}$ F.

accompanying a moderate albuminuria which appeared on the twenty-third day of the disease and disappeared on the twenty-sixth day (Fig. 73). In severe nephritis fever may persist throughout the duration of this complication. In some cases no fever is noted whatsoever.

Before the appearance of the albumin, there is not infrequently noted a considerable increase in the quantity of the urine voided. As a result of this polyuria urination is frequent and may wake the patient from his sleep at night.

Most writers refer to pain in the back as one of the early symptoms of scarlatinal nephritis; this lumbar pain cannot be frequent or severe, at least in children, for it is most rare to hear a complaint in reference thereto. Hæmaturia may be one of the early symptoms to direct attention to the kidneys.

FIG. 73



Scarlet fever. F. O., aged six years. Chart showing pronounced rise of temperature coincident with the onset of albuminuria. Albumin was first found on the twenty-third day.

One of the most characteristic features of scarlatinal nephritis is the *marked pallor of the countenance, with puffiness of the eyelids*. In walking through a scarlet-fever ward one may frequently pick out the nephritic patients by noting this appearance. *Edema* is a particularly common symptom in scarlatinal nephritis. A peculiarity of this complication is the tendency to rapid anasarca. This appears to be much more common in the nephritis of scarlatina than in ordinary Bright's disease. In explanation of this it is stated that the œdema is due not alone to the condition of the kidneys, but also to changes in the lymphatics and bloodvessels of the skin.

The anasarca is accompanied by a pale or alabaster-like appearance of the skin. The swelling usually begins about the eyelids and the ankles, but later the legs, genitalia, and lower portion of the abdomen become affected. In severe cases the entire body may be attacked. A thin and poorly nourished child may become rapidly metamorphosed

into a plump child within a few hours, as a result of the oedematous infiltration. Anasarca, according to Trousseau, is met with in cases of medium severity, rather than those of the most serious forms of scarlatina. Its frequency varies greatly in different epidemics. Barthez and Rilliet observed anasarca in one-fifth of their cases. Some writers have stated that nearly all of their cases were dropsical. Among the 150 cases of scarlet fever referred to above, we did not see a single instance of anasarca, although oedema of the face was not an uncommon symptom.

Anasarca may affect deep seated structures or the serous cavities. The fluid may fill up the peritoneal cavity, giving rise to a pronounced ascites, or the pleural or pericardial sacs may be similarly infiltrated. The soft palate, uvula, epiglottis and arytenoepiglottidean ligaments are more rarely attacked, in the latter case giving rise to oedema of the glottis. In such cases intubation or tracheotomy may have to be performed to prevent suffocation.

Edema of the lungs and brain are extremely apt to be present in cases that terminate unfavorably.

Anasarca may be present in rare cases without albumin being found in the urine. This does not indicate that nephritis is not present, for uræmic symptoms may burst forth suddenly and with great intensity.

Henoch reports the case of a twelve-year-old child admitted to the hospital with oedema of the face and scrotum following scarlet fever. The urine was scanty, but contained neither albumin nor nephritic elements. Two days later convulsions occurred and three days afterward the child died.

THE CONDITION OF THE URINE.—In the so-called febrile albuminuria, the urine contains albumin for a day or two, after which it disappears, perhaps to reappear at the end of the third week. Microscopic examination reveals the presence of cylindroids and occasionally a few hyaline or epithelial casts. Not infrequently red and white blood corpuscles are present. A cloudiness is often seen in the urine, which is due to the presence of mucus resulting from the presence of degenerated epithelium. With the advent of the true scarlatinal nephritis the urine, as a rule, begins to decrease in quantity, although exceptionally there may be for a short time an increased secretion. The urine becomes quite concentrated and contains an abundance of urates, which give a pronounced ring with the nitric acid test. Albumin is found at first in small quantity, but later in larger amount. In bad cases it may constitute half by bulk with the heat test or, indeed, there may be complete coagulation of the urine. At this time hemorrhage from the parenchyma of the kidney may take place, causing the urine to look brownish-red and smoky. Under the microscope will be seen red blood corpuscles, cylindroids, epithelial detritus, and hyaline, epithelial, fatty, and blood casts.

When there is much blood present it will settle as a deep red collection at the bottom of the urine glass. The amount of albumin is correspondingly increased with an augmentation in the quantity of blood.

Exceptionally albumin may be absent for a number of days, although casts are present; on the other hand, a considerable quantity of albumin may be present without urinary casts being found.

The specific gravity varies greatly according to the amount of urine passed. It may be as low as 1004, or as high as 1040 or more; ordinarily it will be between 1020 and 1035. The amount of urine secreted progressively diminishes in severe cases, and there may be complete suppression for a period of twenty-four hours or longer. Cases in which this occurs usually succumb.

The reaction of the urine is almost invariably acid. The quantity of urea excreted varies with the amount of urine, but is usually under 2 per cent.

When dropsy occurs the urine is extremely scanty, high colored, of high specific gravity, and contains an abundance of albumin and casts.

It is not at all uncommon for the albumin to disappear every now and then from the urine, only to reappear in a few days. We have frequently noted this irregularity in scarlatinal albuminuria. In certain cases the albumin appears intermittently in the urine. At other times it is absent at certain periods of the day; this peculiarity has been observed in a considerable number of patients in certain epidemics. This occurs independently of those cases in which albumin is absent while the patient remains in a recumbent position, but reappears when a sitting or standing position is assumed.

These observations make it a matter of importance to carefully examine the urine at frequent intervals. If an examination is made only from time to time, albumin which is intermittently absent or which disappears at a certain time of the day may be completely overlooked. It is a good plan to examine the urine every other day up to the fifteenth day of the disease and then to make daily analyses. The urine should be examined both for albumin and microscopically, and the amount passed and the specific gravity should be ascertained. With the use of very delicate tests small quantities of albumin will doubtless be found which are not recognizable by the usual tests employed. For practical purposes, however, the nitric acid or heat test will suffice.

In cases that tend toward recovery the urine increases in quantity, the blood and casts disappear, and the albumin gradually diminishes.

In our experience the urine in scarlet fever has given a positive *dialysis reaction* in about 25 per cent. of the cases examined. This reaction has little or no diagnostic value.

Aubertain¹ and Roger have each reported cases of scarlatinal albuminuria in which albumin was absent in the mornings while the patient remained in bed, but would appear soon after the patient stood upon his feet. Ten minutes' standing posture in one case would produce an albuminuria lasting about two hours. Exercise in the horizontal position failed to excite the presence of albumin. In some of these cases of *orthostatic albuminuria* a gradual cure takes place; others eventuate in a permanent albuminuria.

¹ L'Albuminurie orthostatique au cours de la néphrite scarlatineuse. *La presse méd.*, 1901.

In some cases of severe nephritis, particularly when the urine becomes greatly reduced in quantity, symptoms of *uræmia* are prone to develop. These usually come on gradually after distinct evidences of kidney involvement, although this is not invariably the case. Indeed, *uræmia* may, in rare cases, supervene without the previous existence of albuminuria. Henoch reports such a case; on the twelfth day of scarlatina, in a four-year-old child, intense right-sided convulsions and stupor developed; examination of the urine on the previous day had failed to show albumin. The patient was catheterized on the development of the symptoms, and a considerable quantity of albumin was then found.

Ordinarily the first symptoms in a patient about to develop *uræmia* are vomiting and, at times, diarrhoea. This is doubtless an effort on the part of nature to eliminate some of the retained poisons through these channels. Leichtenstern claims that one of the most frequent modes of onset of scarlatinal *uræmia* is the development of pronounced dyspnoea associated with rapid heart action. There is usually some elevation of temperature, which, in bad cases, may become excessive and reach 106° or 107° F. But the symptoms referable to the nervous system dominate the clinical picture. There are frequently intense headache, tinnitus aurium, and somnolence or stupor, with occasionally sudden loss of vision. These symptoms are rapidly followed by convulsions. The convulsive movements may be partial, that is, limited to one set of muscles, as those about the jaws, in which event there may be a tonic contraction; in other instances they are unilateral or general, affecting the entire body. When the convulsions are limited to certain sets of muscles consciousness is usually preserved, but when there is a general epileptiform seizure it is followed by coma, at least for a time. The convulsive attacks may be of brief duration, lasting but a few minutes, or they may persist for an hour or more. There may be a single seizure, although more commonly there is a succession of convulsions upon the same or successive days.

When the convulsions are severe and protracted, death may result from exhaustion, cerebral hemorrhage, or œdema of the lungs. In other cases a fatal termination comes on later, the patient lapsing into a progressively deepening coma. In some cases a gradual oncoming stupor may be the only pronounced symptom of *uræmia*.

In favorable cases the convulsions cease, the stupor disappears, the urine increases in quantity, and the patient emerges from the crisis.

The amaurosis which develops from time to time in *uræmia* usually disappears when the convulsions cease, but the blindness may continue for several weeks, ultimately ending in complete recovery. In some cases aphasia and hemiplegia may develop during *uræmic* convulsions and disappear when convalescence is established.

In rare instances patients may become *maniacal* after *uræmic* attacks. Wagner¹ saw a patient who had eleven convulsive seizures, each one being followed by the wildest mania; although the temperature registered 107.6° F., the patient recovered.

¹ Quoted by von Jürgensen, loc. cit.

The first of the two cases is a woman, aged 45, who had been suffering from chronic nephritis for many years. She had been treated with various remedies, but without success. She was admitted to the hospital in the month of June, 1907, with the following symptoms: edema of the face and legs, headache, and general weakness.

On admission, the patient was found to be in a state of moderate to severe toxemia. The blood pressure was 160/100 mm. Hg. The urine was found to contain albumin and casts. The patient was treated with a low protein diet, and the administration of sodium chloride. The edema subsided, and the patient was discharged in the month of August, 1907. She was followed up for several months, and was found to be in good health.

The second case is a man, aged 55, who had been suffering from chronic nephritis for many years. He had been treated with various remedies, but without success. He was admitted to the hospital in the month of June, 1907, with the following symptoms: edema of the face and legs, headache, and general weakness.

On admission, the patient was found to be in a state of moderate to severe toxemia. The blood pressure was 160/100 mm. Hg. The urine was found to contain albumin and casts. The patient was treated with a low protein diet, and the administration of sodium chloride. The edema subsided, and the patient was discharged in the month of August, 1907. He was followed up for several months, and was found to be in good health.

Both cases suggest a form of nephritis after water fever, which is not uncommon. The first case is a woman, aged 45, who had been suffering from chronic nephritis for many years. She had been treated with various remedies, but without success. She was admitted to the hospital in the month of June, 1907, with the following symptoms: edema of the face and legs, headache, and general weakness.

It should be noted that the above cases were not typical, and careful microscopic examinations of the urinary sediment were uniformly made for months after subsidence of edema, it would doubtless be found that a larger proportion of cases eventuate in chronic nephritis than has been supposed.

Many of these patients have structurally damaged kidneys, which at some future period, as a result of a variety of causes, may be reawakened into activity. The practical lesson to be borne in mind is that the urine of patients convalescent from scarlatinal nephritis should be

carefully examined from time to time, and the diet and mode of life regulated accordingly.

Scarlatinal Rheumatism (Synovitis Scarlatinosa).—In the absence of conclusive evidence that acute articular rheumatism is a specific morbid process due always to the same infectious agency, we are justified in adhering to the old term “scarlatinal rheumatism.” The attempt to distinguish between a scarlatinal synovitis and a complicating rheumatism is scarcely warranted by our present knowledge of the subject. Synovitis and arthritis occurring in the course of scarlet fever are frequently associated with other phenomena, such as endocarditis, pericarditis, pleurisy, etc., which are common rheumatic complications.

The frequency of joint involvement in scarlatina appears to vary in different countries and in different epidemics. Trousseau says: “By minute interrogation, and by carefully examining and applying a certain degree of pressure to the joints, articular pains are found to be present in about one-third of the cases (of scarlatina). It is important to know this; for acute affections of the joints, general arthritis, pericarditis, and endocarditis frequently occur during the course of the disease.”

Ashby observed synovitis to occur 20 times among 900 cases of scarlet fever. Koren,¹ of Christiana, noted scarlatinal synovitis of a mild type 27 times in 426 cases (6.3 per cent.) of scarlet fever in the epidemic of 1875–77.

Vogl appears to have observed an unusually large number of cases of joint complications in scarlatina. He is authority for the statement that articular involvement occurred in 13.6 per cent. of the cases in the epidemic of 1884–85, and in 10.6 per cent. in 1894–95.

Hodger² saw 217 instances of scarlatinal synovitis among 3000 cases of scarlet fever, or 3.2 per cent.

It is seen from the above figures that the frequency of this complication varies from about 3 to 13 in 100 cases. Our personal experience would lead us to regard the first figure (3 per cent.) as representing more nearly the average incidence of this complication.

Two forms of joint involvement are recognized—a simple serous synovitis and a purulent or suppurative arthritis. The mild form is fortunately far more common than the suppurative variety. Articular involvement may occur at any period of the disease, but is most common during the stage of desquamation in the second or third week of the disease. The wrists and fingers are the joints most often attacked, although the ankles and toes not infrequently participate in the process. Sometimes the larger joints, such as the shoulders and knees, become involved. The usual symptoms are pain, stiffness, and swelling. Redness may or may not be present. Trousseau states that scarlatinal rheumatism is usually mild and of short duration, is commonly localized, and when it disappears does not tend to return. We have seen cases

¹ See Johannsen, *loc. cit.*, p. 195.

² See Eichhorst's *Spec. Pathol. und Therapie*, Leipzig, 1897, p. 241.

in which there were periods of disappearance and of recurrent involvement. Scarlatinal rheumatism is frequently, although not always, attended with a rise of temperature which commonly reaches 101° or 102° F.

In mild cases the articular inflammation subsides in the course of three to five days. In more severe cases it may last for weeks.

Suppurative Arthritis.—Suppurative arthritis is a rare complication of scarlet fever, and usually occurs late in the course of the disease. The joint becomes painful, swollen, hot, and reddened; the fever is high, the patient prostrated, and all of the usual symptoms of pyæmia are present. One or several articulations may be involved. In the vast majority of cases a fatal termination supervenes. In rare instances, through surgical intervention, or even at times without, recovery takes place after a long and tedious illness, but with serious impairment of the functional activity of the joints involved.

We have seen scarlatinal rheumatism associated in one case with a severe endocarditis and a recurring geographic erythema of the trunk and extremities, and in another fatal case with endocarditis, pleurisy, and hemorrhagic purpura.

In persons of scrofulous habit a scarlatinal synovitis may, after a long course, eventuate in tuberculosis of the joint (white swelling).

In rare cases of scarlet fever the sheaths of tendons may undergo inflammation (*tenosynovitis*), which commonly terminates in suppuration. In other cases periarticular abscesses may occur and rupture into one of the large joints.

Cases of *periostitis* and *ostitis* have been reported, involving particularly the petrous portion of the temporal bone, the nasal bones, and the cervical vertebræ.

Brück¹ describes a form of scarlatinal myositis, which attacks most commonly the lumbar, pectoral, abdominal, and intercostal muscles, and which is characterized by pain and soreness and moderate rise of temperature.

Purpura Hemorrhagica.—It is important to distinguish between true hemorrhagic scarlatina and secondary purpura developing during the course of the disease. The former condition appears, as a rule, at the outset, and is characterized by constitutional symptoms of great intensity and malignancy, associated with hemorrhages into the skin and from the mucous membranes.

Purpura hemorrhagica comes on usually after the subsidence of the acute scarlatinal symptoms and not infrequently during convalescence. Most cases develop during the second or third week, and most commonly from the fourteenth to the twentieth day. The patient loses appetite, is apathetic, and may have some rise of temperature. Nose-bleed is often one of the first symptoms; soon pinhead-sized purpuric spots appear upon the skin of the trunk, extremities, or face; the gums become swollen and bleed; the urine contains blood, and hemorrhage may take

¹ Petersb. med. Presse, 1896, No. 18.

place from the stomach and bowels. A marked pallor soon develops, the patient becomes prostrated, and, in severe cases, death takes place from loss of blood, hemorrhage into the brain, or exhaustion.

Albuminuria is usually present, even when the urine is free of blood.

In mild cases the hemorrhages from the various mucous membranes cease after a short time, and the patient, although intensely anæmic, recovers.

These secondary purpuras are not seen alone in scarlatina, but in other infectious diseases, such as influenza, rheumatism, smallpox, etc. They are probably due to some secondary infection which destroys either the integrity of the blood or the vessel walls. We have seen two cases of hemorrhagic purpura complicating scarlatina.

A three-year-old child, suffering from a well-marked scarlatina, developed late in the course of the disease swelling of the joints, diffuse

FIG. 74



Purpura hemorrhagica associated with pleurisy, endocarditis and joint trouble, complicating scarlet fever. Fatal termination.

ecchymotic patches upon the face, trunk, and extremities, and endocarditis. The patient after some days' illness died. Autopsy showed vegetations upon the mitral and aortic valves, a right-sided pleurisy, and hemorrhages into the mediastinal and peritoneal cavities.

The second case was a girl, aged eight years, who, upon the seventeenth day of a scarlatina of average severity, became apathetic, had slight rise of temperature, and nose bleed. The following day, small, pinpoint petechiae appeared upon different parts of the body, bleeding occurred from the gums, and an abundance of blood was found in the

urine. The bleeding continued for a few days, but ceased under treatment and the patient made a good recovery. A pronounced anæmia persisted for a few weeks. Albuminuria was present even after the cessation of hæmaturia.

Although this complication is uncommon, a number of cases have been published. Biss¹ reports the case of a boy, aged three and one-half years, who suffered from a severe attack of scarlet fever complicated by double otitis media. On the nineteenth day after admission to the hospital he developed an extensive eruption of pinpoint hemorrhages over the trunk and limbs, vomited a half-pint of blood, passed a similar quantity by the bowel, and rapidly succumbed. Autopsy showed the kidneys to be "transformed almost entirely into fat."

Murray² saw a two-year-old colored child develop scarlatina after an operation for hernia. On the ninth day of the attack there occurred bleeding from the kidneys, bowels, stomach, nose, and gums, and hemorrhages into the skin and conjunctivæ. The red corpuscles numbered 2,000,000 per cubic centimetre. Urine contained blood and epithelial and hyaline casts. Death took place on the fourteenth day.

De Boinville³ places on record the case of a boy, aged four and one-half years, who, on the sixteenth day of scarlet fever, had hemorrhages from the nose and hemorrhagic spots on the scalp and about the knees. Although the amount of blood lost was small, the epistaxis could not be checked and the patient died five days later.

Phillips⁴ reports the case of a girl, aged fourteen years, suffering from scarlet fever, who had a recurrent rash on the fourteenth day, and swelling of the joints on the twentieth day; six days later petechial patches on the chest and legs and free bleeding from the nose, gums, and kidneys. Patient had albuminuria and acute dilatation of heart, but recovered.

Gangrene.—Mention has already been made of the sloughing of the tissues of the neck, which occasionally accompanies cellulitis and abscesses. The muscles and large bloodvessels of the neck may be exposed by gangrene of the overlying skin.

Gangrenous stomatitis, or *noma*, is also seen at times after scarlatina, although it is much rarer than after measles. Apart from these conditions, a form of spontaneous gangrene is, in rare instances, observed during the course of scarlatina. When seen, gangrene usually develops during the second or third week of the disease, and usually attacks the extremities. In most of the reported cases the condition has been attributed to embolism. There appear first bluish discoloration, pain, and coldness, and then hemorrhagic extravasation into the skin. In some of the reported cases the gangrene was so deep and extensive as to necessitate amputation of the affected member.

¹ Lancet, August 2, 1902, p. 256.

² Case of Scarlet Fever with Purpura, Lancet, February 11, 1893, vol. i.

³ A Peculiar Case of Scarlatina Hemorrhagica, Lancet, August 9, 1903. This case is evidently a purpura hemorrhagica, and not one of true hemorrhagic scarlatina.

⁴ Scarlet Fever with Relapse; Acute Rheumatism and Purpura Hemorrhagica; Recovery. London Lancet, 1893, vol. ii.

Cases of gangrene have been reported by Blanpain,¹ Hudson,² Küster,³ and Chapin.⁴

Wood and Arrigoni⁵ have reported cases of gangrene affecting the genitalia, and Wilson⁶ a case of gangrene of the face occurring three weeks after convalescence from scarlatina.

Pearson and Littlewood⁷ report the case of a boy, aged four years, who, after an ordinary scarlet fever, on the eighth day developed small, hemorrhagic discolorations of the skin of both legs. In a few days the legs became livid, first upon the feet, thence spreading upward. The femoral pulsation was lost, the legs became cold, intermittent pain occurred, and lines of demarcation formed about three inches above the knees. At the same time slight dilatation of the heart was discovered. On the twenty-third day of the disease the right leg was amputated, and, a week after, the left. The patient recovered. Embolic and thrombotic clots were found in the bloodvessels of the amputated limbs.

Buchan⁸ reports the case of a boy, aged thirteen years, whose scarlatinal rash on the second day exhibited a bluish appearance on the legs. A few days later the veins, especially at the apex of Scarpa's triangle, stood out quite prominently. Hemorrhages occurred into the skin of the legs, particularly the right; there were also hæmaturia, nose-bleed, and hæmoptysis. The lower part of the right leg became mummified and a definite line of demarcation formed just above the knee, where an amputation was performed. The patient made a rapid recovery.

We recall a child treated in the Municipal Hospital in 1900, who developed gangrene about the third week of a severe scarlatina. Ecchymotic patches developed upon the leg, followed by rather superficial sphacelation of the tissues. A few days later one hand became blue and cold, and shortly after this the other hand became similarly affected. The radial pulse was lost and both hands assumed an indigo-blue color. Before actual gangrene could take place the child, who was greatly prostrated, died. The gangrene in this case was doubtless due to embolism (Fig. 75).

Skin Complications.—Reference has already been made to the various abnormalities of the rash of scarlet fever, including an excessive development of miliary vesicles. It remains to discuss the occasional complicating skin disorders which are quite apart from the scarlatinal process.

¹ Scarlatine; gangrene spontanée des membres; embolies; autopsie. *Arch. Med. Belges, Brux.*, 1869, 2, ix. pp. 324-331.

² Scarlatina Resulting in Mortification of the Right Limb, and Successful Amputation. *Transactions of the Ohio Medical Society*, 1858.

³ Spontan. Gangrän des Unter-schenkels nach scarlatina; Amputatio Femoris; Tod., *Kassel*, 1876 and 1878.

⁴ An Unusual Result of Scarlet Fever; Embolus; Gangrene; Amputation. *Medical Age, Detroit*, 1884, xi. p. 205.

⁵ Quoted by Thomas.

⁶ Reviewed in *Archiv f. Kinderheilk.*, 1898, p. 418.

⁷ Dry Gangrene of Both Legs; Double Amputation, 1897, 11, p. 84.

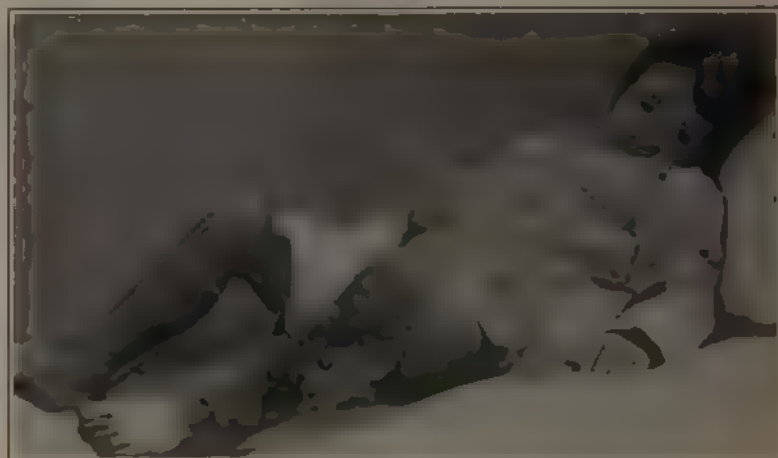
⁸ *Lancet*, October 5, 1901, p. 915.

Febrile *herpes* occurs every now and then during the invasive stage of the disease. The patches develop usually about the mouth, although they may be situated about the cheeks or ears. While herpes is not very frequent in scarlet fever it is more commonly seen than in smallpox or measles.

Urticaria is not an infrequent accompaniment of scarlet fever, although it cannot be considered as bearing any special relation to the disease. It may be seen early or late in the course of the illness, and is usually neither extensive nor protracted. This complication is doubtless due to the presence in the blood of some accidental toxin or drug.

Blebs may occasionally develop upon the skin as a result of a coalescence of neighboring miliary vesicles in intense rashes. Thomas says that they may reach the size of hazel-nuts. Bullæ may also occur upon patches which are destined to terminate in gangrene of the skin. Some

Fig 75



Gangrene of the skin complicating scarlet fever. Patient developed gangrene of both hands and died.

authors speak of the occurrence of pemphigus, particularly in certain epidemics. These are, in all probability, not true instances of pemphigus, but of bullous dermatitis of septic origin.

We have occasionally seen cases of localized necrosis of the skin in small areas, a condition analogous to the so-called *varicella gangrenosa*, but better designated *dermatitis gangrenosa*. Fig 76 shows this condition upon the knees of a young boy.

Ecceema may occur as a complication of scarlatina, but is more apt to develop as a sequel. Intense desquamation may leave the skin dry, harsh, and fissured, and the seat of eczematoid patches; these may persist for some time after convalescence. In other cases a purulent discharge from the ears or nose may give rise to an impetiginous eczema in the region of these orifices, the skin becomes moist and covered with crusts as the result of the irritating and infective discharges.

Cutaneous abscesses may occur upon any portion of the integument. This complication is uncommon, usually occurring in septic cases. We recall an adult patient in whom a large number of small abscesses occurred in the skin.

Furuncles may develop during an attack of scarlet fever, although they are more apt to appear after the termination of the disease. In a severe case seen recently they complicated an unrecognized and untreated nephritis, after convalescence from scarlatina had taken place.

Phlebitis.—Phlebitis appears to be a rare complication of scarlet fever. The veins of the neck, upper extremities, and cranial cavity are those most apt to be affected. The cases in which this complication develops are usually severe; the phlebitis not uncommonly occurs in the neighborhood of suppurating glands or abscesses.

FIG. 76



Dermatitis gangrenosa occurring in a severe case of scarlet fever. (This condition is analogous to the so-called "varicella gangrenosa.")

Cases have been reported by Rees,¹ Hofnagels,² von Jürgensen,³ and Moizard and Ulmann.⁴ The latter writers were able to collect from the literature but four cases of phlebitis after scarlatina. In their own case, a phlebitis of the right axillary and humeral veins, cultures demonstrated the condition to be due to a streptococcic septicemia.

Roger⁵ has recently published an account of a woman, aged forty-nine years, who died on the eleventh day of a severe scarlatina, after suffering for three days with a phlebitis of the crural vein. Autopsy showed vegetations on the auricular surface of the mitral valve.

Alimentary Canal. Reference has already been made to the condition of the mouth and throat in scarlatina.

¹ Fatal Phlebitis After Scarlet Fever, London Lancet, 1862, II, p. 63.

² Ann. Soc. de méd. d'Anvers, 1848, ix, pp. 333-345.

³ La phlébite scarlatineuse, Archiv. de méd. des enfants, 1899, vol. II, No. 10, p. 601.

⁴ Loc. cit., p. 362.

⁵ Loc. cit.

The vomiting, which is so common at the beginning of scarlet fever, is seldom sufficiently intense or protracted to unfavorably influence the course of the disease. In hemorrhagic scarlet fever the material vomited may contain blood. At a later stage of the disease vomiting may be an expression of nephritis, or, when repeated, of an oncoming uræmia. Thomas says that severe gastralgia, persistent and often bilious vomiting, and great sensitiveness of the stomach to all food, occur in some cases; we have never observed such severe gastric symptoms. Pathological changes have frequently been described as occurring in the walls of the stomach, but it would seem that in many cases these do not give rise to pronounced symptoms.

In the period of invasion and the early eruptive stage it is not at all rare for *diarrhœa* to manifest itself. In ordinary cases this is due to a simple catarrhal *enteritis* which yields of its own accord or to simple treatment. In very severe cases of scarlatina, however, the bowel movements may be frequent and profuse, and accompanied by pain and tympanitic distention. If the diarrhœa is protracted the tongue becomes dry, the eyes sunken, and the face pinched. This complication under such circumstances is much to be feared, leading, as it may, to exhaustion and a fatal termination.

Joel¹ saw a patient in whom severe gastrointestinal symptoms and high fever were the most conspicuous symptoms; slight angina, subsequent scaling, and an attack of scarlet fever in the sister made the diagnosis clear.

In the later stages of the disease there is occasionally encountered a *dysenteric* condition, characterized by frequent, small, bloody, or catarrhal stools and painful tenesmus.

Litten² speaks of diarrhœas of *typhoidal character*. 'There is marked distention of the abdomen, and critical hemorrhages from the bowel may occur. The stools are liquid, of a pale-yellow color, and dotted with whitish specks. This condition is associated with a protracted remittent fever, dry tongue, pronounced apathy, and later renal complications. When the patient recovers, convalescence is long drawn out. On autopsy in these cases there is enlargement of the spleen and the mesenteric glands, swelling of Peyer's patches and of the solitary follicles, the latter at times exhibiting erosion.

Liver.—The liver is generally increased in size, the inferior border often extending below the false ribs. Hepatic enlargement is, however, not constant, and the liver may, in severe cases, be much diminished in size as a result of degeneration and atrophy. Jaundice is not a common symptom, but it is encountered, according to some authors, with especial frequency in certain epidemics.

Mild jaundice has no special significance, but severe cases may indicate extensive fatty degeneration of the liver.

Roger³ says that lesions of the liver often explain different forms of delirium and modifications of temperature. He mentions the case of a

¹ Quoted by Thomas.

² Loc. cit., p. 1055.

³ Charité-Annalen, Bd. vii. p. 128.

confirmed nineteen-year-old alcoholic suffering from scarlatina, who had severe delirium of the type of delirium tremens early in the disease. The liver was large and palpable; the urine was free of albumin. The patient died three days later, with a temperature barely above normal. The liver at autopsy was found to be huge and completely degenerated.

Respiratory Organs.—The larynx may become involved as a result of a secondary diphtheria or a membranous inflammation of streptococcic origin, although the latter is much rarer than in measles. Œdema of the glottis results at times from extension of inflammation, and on other occasions from nephritis.

Perichondritis of the larynx is a rare and fatal complication. According to Kraus¹ it occurs about once in 200 to 250 cases of scarlatina. Rauchfuss saw 4 cases among 903 cases of scarlatina, and Leichtenstern 2 cases among 467 patients. Its development may necessitate the performance of intubation or tracheotomy.

Pulmonary complications are much less common in scarlatina than in measles. The *bronchial tubes* and *lungs* are nevertheless, according to Hensch, much more frequently involved in bad cases than is generally believed. These lesions are masked by the severe constitutional symptoms, and are often not discovered until autopsy. In a series of 98 fatal cases of scarlatina, reported by McCollom,² 15 were due to bronchopneumonia.

As would naturally be expected, pulmonary complications are commoner in infants than in older children and adults. Roger³ gives the following morbidity and mortality statistics of pulmonary complications in scarlatina according to age:

Scarlatina.	No. of patients.	Cases of pneumonia.	Mortality.
First infancy . . .	56	6 (10.7 per ct.)	5 (8.9 per ct.).
Childhood . . .	430	6 (1.3 per ct.)	2 (0.4 per ct.).
Adults . . .	1727	4 (0.2 per ct.)	3 (0.1 per ct.).

All of the pneumonias in the infants were bronchopneumonias. Four of the children of the second group had bronchopneumonia, and two had apical pneumonia. Bronchopneumonia occurred in two adults.

Bronchopneumonia in severe cases appears usually during the first or second week. Hensch remarks: "We found bronchitis and bronchopneumonia in nearly all the severe cases and also repeatedly during life."

Lobar Pneumonia.—Lobar pneumonia may develop during the height of the disease, or more commonly after nephritis has manifested itself. The upper lobes are more often affected than other parts of the lungs.

Œdema of the Lungs.—Œdema of the lungs is by no means a rare complication when the kidneys are severely affected and a general dropsy exists. Serous transudation into the lungs may occur rapidly and lead to sudden death.

Involvement of the *pleural cavities* in scarlatina is uncommon.

¹ Prag. med. Wochenschr., 1899, pp. 29 and 30.

² Quoted by Corlett, loc. cit.

³ Loc. cit, p. 983.

Pleurisy may develop in association with a lobar pneumonia or it may occur independently thereof. The process may be dry or accompanied by serous or purulent exudate; scarlatinal pleurisies show a pronounced tendency to eventuate in *empyema*, a complication which adds much gravity to the disease. However, desperate cases may at times terminate favorably, as is evidenced in a remarkable case of Trousseau, who drew off from the chest of a fourteen-year old girl 750 grams of pus, the patient making a complete recovery.

Thomas says all forms of scarlatinal pleurisy are characterized by rapid development and by but slight local disturbance, even when the affection is very intense. The effusion is usually present only upon one side.

Pleural involvement is more frequent in cases complicated by nephritis. It is especially apt to accompany scarlatinal rheumatism. We have already referred to a patient treated in the Municipal Hospital, who had purpura, endocarditis, synovitis, and a fibrinous pleurisy.

Furbringer regards exudative pleurisy as a frequent complication, occurring, in his experience, in 5 per cent. of cases of scarlatina. Johansen, of Norway, found, among 688 deaths from scarlet fever, but 3 that resulted from pleurisy.

Nervous System.—While the onset of scarlatina is attended in severe cases by pronounced nervous symptoms, these subside if the course is favorable, and do not add to the gravity of the disease. The early cerebral manifestations are in part due to the scarlatinal poison and in part to the high fever. Headache and delirium may be present in ordinary cases, but convulsions and coma presage an attack of great severity.

Later in the disease severe nervous symptoms, such as delirium, convulsions, coma, sudden blindness, etc., may develop as a result of uræmia.

Hemiplegia.—Hemiplegia may occur early from a cerebral hemorrhage during the invasive convulsions, or it may come on at a later date as the result of embolism. Taylor¹ reports a right hemiplegia resulting from embolism of the middle cerebral artery; the patient succumbed later to diphtheria.

Addy² saw a case of partial hemiplegia with amnesia after scarlatina.

Meningitis.—Meningitis usually results from extension of inflammation and infection from the middle ear or the nasal sinuses. We have already referred to a case of purulent meningitis of the base of the cerebellum which we observed after a purulent otitis media. Roger³ saw a twenty-three-year-old man in whom a severe purulent rhinitis complicating scarlatina was followed by meningitis. At autopsy the left frontal lobe of the brain was covered with purulent plaques and the left sphenoidal sinus contained pus. The presence of the streptococcus in pure culture was demonstrated. Similar cases have been

¹ Medical Times and Gazette, London, 1890, ii. p. 606.

² Glasgow Medical Journal, 1890-95 8. xiii. pp. 463-465.

³ Loc. cit., p. 850.

reported by other observers. Baudelocque¹ reports a case of meningo-encephalitis characterized by headache, vomiting, and convulsions, followed by coma and the loss of speech, hearing, and sight. Althous² reports a case of spinal meningitis with consecutive lateral and posterior sclerosis.

Incomplete Paraplegia.—Cases of incomplete paraplegia have been described by Demange,³ Roger, and others. Roger says that among 2213 patients with scarlatina 4 cases of incomplete paraplegia were observed. Three women had for about a week great difficulty in standing up or walking. The fourth patient was a man who on the second day of the disease had paralysis of the soft palate. Later the two legs and the right arm became affected; the palsy passed off in ten days. Cultures from the throat excluded the possibility of diphtherial infection.

As has already been stated, *facial palsy* occurs occasionally from involvement of the facial nerve in the bony roof of the middle ear.

Insanity.—Insanity has been reported as a complication and sequel of scarlatina. The mental aberration is usually temporary, but may in some cases persist after convalescence. Mitchell,⁴ Rabuske, and Wagner have each reported attacks of acute mania in scarlet fever, the mania in the last-named case following uræmic convulsions.

Carrieu⁵ records a case of dementia and Brill a case of scarlatinal insanity with epilepsy. Wildermuth,⁶ in a report of 187 cases of epilepsy, states that 12 cases followed attacks of scarlet fever.

Multiple Neuritis.—Egis⁷ reports a case of multiple neuritis following scarlatina in which there was an ataxic gait and paralysis of both peroneal nerves. But two other cases of multiple neuritis could be found in literature.

Tetany.—Steffen⁸ reports a case of tetany in a young girl suffering from scarlatina; an attack was noticed after each bath. Kühn-Ulsar⁹ mentions a case of tetany in a boy, aged four and one-half years, suffering from scarlet fever. For six weeks muscular spasms and stiffness were noted, at times limited in extent and at other times general. Trismus was present for fourteen days. The patient gradually recovered.

Bones.—Necrosis of the petrous portion of the temporal bone and of the ear ossicles occurs in severe cases of purulent otitis media. Necrosis of other bones sometimes takes place. Brown¹⁰ reports a case of necrosis of the lower maxilla after scarlet fever, and Weickert¹¹ reports a case in which both jaws were thus affected.

Neumark¹² reports 30 cases of acute infectious *osteomyelitis*, of which 5 followed scarlet fever.

¹ Gaz. des. hôp. de Paris, 1837, xl. pp. 197-199.

² Bull. Soc. anat. de Paris, 1874, pp. 503-9.

³ Edinburgh Medical Journal, 1881-82, xxvii. pp. 721-24.

⁴ New England Medical Monthly, 1882-83, li. pp. 55-58.

⁵ Archiv f. Kinderheilk., 1900, xxviii.

⁶ Berliner klin. Wochenschrift, 1899, No. 39, p. 855.

⁷ London Lancet, 1844, i. p. 220.

⁸ Deutsche Klinik, Berlin, 1854, vi. p. 22.

⁹ Brit. Med. Journal, 1881, i. p. 50.

¹⁰ Quoted by Holt, loc. cit.

¹¹ Jacobi's Festschrift, 1900, p. 83.

¹² Archiv f. Kinderheilk., Bd. xxii.

Sequelæ.—But few words will be devoted to the sequelæ of scarlatina, as they represent merely a continuation of the complications or disabilities resulting from structural damage.

A weakened and anæmic state of the system may develop after scarlatina as after many other infectious diseases; the patient is thus lowered in resisting power and rendered more susceptible to the other infectious diseases. There is, however, no such increased susceptibility to tuberculosis as exists in patients recovering from measles.

The various organs of sense may bear for a long time and in some cases forever the marks of a cruel scarlatinal attack. The mucous membrane of the eyes, throat, and nose may show persistent pathological alteration.

It is the ears, however, that most frequently exhibit permanent damage. It is largely because of injury to the sense of hearing that scarlatina is so feared by the laity. A chronic purulent otitis media may persist after scarlatina and lead at a remote date to mastoid or intracranial disease. Destructive changes involving the middle ear and the contained ossicles may cause auditory disability, varying in degree from slight impairment of hearing to complete deafness. When this occurs very early in life the loss of this sense may lead to deaf-mutism.

As has already been suggested, the damage to the kidneys is often more than a transitory one. In a certain proportion of cases albuminuria will persist and eventuate in a chronic Bright's disease. In other cases the kidneys are functionally normal, but are rendered more susceptible to subsequent burdens or infections.

Various cutaneous diseases, such as furuncles, eczema, etc., may follow in the wake of scarlatina.

Reference has already been made to certain psychic disturbances, such as mania and melancholia, which may persist after scarlatina.

Chorea.—Chorea may develop a few months after convalescence is established. This sequel is not of great frequency. Carlslaw reports only 3 cases of chorea following 533 cases of scarlet fever, and Priestley¹ 13 cases after 5355 attacks of scarlet fever.

THE BACTERIOLOGY OF SCARLET FEVER.

Within the past quarter of a century numerous investigations have been undertaken to discover the specific cause of scarlet fever. That the disease is produced by a contagium vivum and that every case of scarlet fever receives its infection from a previous one are propositions which command general acquiescence.

The exciting cause of the disease is certainly micro-organismal, but the identification of the causal parasite is still shrouded in mystery.

As early as 1762, Plenciz,² of Vienna, attributed the cause of scarlatina to living corpuscles. Hallier³ in 1869 was one of the first observers

¹ British Medical Journal, September, 1897, p. 805.

² Quoted by Bergé, loc. cit.

³ Jahrbuch f. Kinderh., N. F., II., 1868, 1869.

to search for the microscopic cause of the disease. With the crude magnifying lenses at his disposal he found a micrococcus in and about the blood corpuscles which he regarded as the morbid agent of the disease.

One year later Hoffman examined the sweat of scarlatina patients and discovered the presence of a micrococcus.

In 1872 Coze and Feltz¹ found in the blood of scarlet-fever patients bacteria 6 microns long, which caused the death of rabbits when inoculated.

Riess² in 1872 found certain alleged lower forms of life in the blood, but failed to prove anything by cultures or inoculations.

In 1875 Klebs found, in the substance of an inguinal gland of a patient suffering from scarlet fever, a sphere made up of micrococci which later changed their form. To this organism he gave the name "monas scarlatinusum."

Tschamer³ in 1879 claimed that scarlatina was caused by a cryptogamic organism, designated by him the "verticillium candelabrum," which is found upon rotten wood. He regarded this as one stage of development of the micrococci found by him in the blood cells, scales, and urine.

In 1882 Eklund⁴ found bodies in the urine of scarlet-fever patients which he called "plax scindens." He found similar organisms in the soil, in water, and on mouldy walls. Children living in the vicinity of such excavated soil were observed to contract scarlatina.

Octerlony observed these same bodies in the blood and urine of scarlatina patients.

In 1883 Pohl-Pincus⁵ found cocci in the epidermic scales and also on the soft palate.

Klamann⁶ made similar observations in the same year.

In 1885 Fraenkel and Freudenberg⁷ isolated a streptococcus from the liver, kidney, and spleen in three fatal cases of scarlet fever.

Babes found in 18 out of 20 fatal cases of scarlet fever a streptococcus which he regarded as a variety of the streptococcus pyogenes.⁸

Loeffler in 1884 isolated the streptococcus from false membrane in the throats of scarlatinal patients.

In 1885 Power⁹ noted a severe epidemic of scarlet fever in London which began among the patrons of the Hendon farm who were receiving milk from cows which were suffering from a peculiar disease.

Klein¹⁰ investigated the circumstances of the epidemic. He found that the disease in the cows was transmitted from one to another, and that

¹ Recherches cliniques et expérimentelles sur les mal. infect., Paris, 1872.

² Quoted by Bourges, Les recherches microbiennes dans la scarlatine. Gaz. hebd. de méd. et de chir., March 28, 1891.

³ Centralz. f. Kinderh., 1878, 1879, ii.

⁴ Quoted by Bourges.

⁵ Centrablatt f. die med. Wissen., 1883, xxi.

⁶ Allgemeine med. Centralz., 1883, lli.

⁷ Quoted by Bergé, Pathogénie de la scarlatine, Paris, 1895.

⁸ Quoted by Bergé.

⁹ Milk Scarlatina, London, Report of the Medical Officer of Local Government Board, February, 1885, 1886.

¹⁰ The Etiology of Scarlatina, Proceedings of the Royal Society of London, 1887, xlii.

it began with fever, followed in two or three days by swelling of the eyes. From the fourth to the sixth day there appeared an eruption, oculonasal catarrh, cough, and rapid breathing. Desquamation occurred about the third or fourth week, with loss of hair. In severe cases sore throat and enlargement of the submaxillary glands were present. On the fifth or sixth days several vesicles appeared upon the udders, which dried into crusts and fell off about the fifth or sixth week. Diplococci sometimes arranged as streptococci were found in these lesions. Klein, in studying the blood of scarlatina patients, found from the fourth to the sixth day of the disease, in 4 out of 11 cases, a streptococcus of the same character as that obtained from the Hendon cows. He regarded this as the cause of the disease, and looked upon the disorder in the cows as bovine scarlatina.

Klein's conclusions were attacked by Duclaux, by C. B. Brown, and also by Crookshank. Crookshank¹ saw an analogous epidemic among cows in Wiltshire from which no scarlet fever was spread. The disease was recognized by him as cowpox. Both Crookshank and Thin contended that the streptococcus found by Klein was the ordinary streptococcus of suppuration.

In 1887, Edington,² working with Jamieson, isolated from the scales and blood of scarlet-fever patients a bacillus which he regarded as the cause of the disease. The organism was quite uniformly found in the blood after the third day and in the scales after three weeks. This so-called bacillus scarlatinæ was motile, grew in long threads, and fluidified gelatin. Inoculations of rabbits and guinea-pigs produced fever and an erythema followed by desquamation.

Brown later demonstrated this bacillus in the scales of ordinary dermatitis. A committee of the Medico-Chirurgical Society of Edinburgh investigated the claims of Jamieson and Edington, and was able to find the bacillus in but 3 of 10 cases of scarlet fever; of nine blood cultures results were obtained in four; cultures from scales were negative and inoculation experiments were without result.

In 1889 Madame Raskin³ read before the St. Petersburg Congress a communication in which she described a peculiar micrococcus which was found in the blood cells at the beginning of scarlet fever. It was likewise discoverable in the internal organs, skin, and mouth at autopsy. It killed rabbits and guinea-pigs, but did not induce symptoms of scarlet fever.

In 1893, Fiessinger⁴ announced his belief that the streptococcus was the cause of scarlet fever.

Dowson⁵ in the same year expressed the opinion that scarlet fever was due to the streptococcus and that the tonsil was the seat of the primary infection.

This assumption was later championed by Bergé and by Lemoine.

¹ Communication to the Pathological Society of London, 1887.

² Jamieson and Edington, *British Medical Journal*, 1887, i.

³ *Centralblatt f. Bakt. u. Parasit.*, 1889, v.

⁴ *Med. Chron.*, Manchester, 1893, 1894, xix. p. 217.

⁵ *Semaine médicale*, July, 1896.

Bergé,¹ in a brochure published in 1895, discusses at length the nature of scarlet fever and formulates the following conclusions:

1. Ordinary scarlatina is a local infection of the tonsils. The scarlatinal eruption (exanthem and enanthem) is the result of a toxic erythrogenic action of the microbic poisons secreted in the infected tonsils.

2. An imposing array of evidence points to the streptococcus in one of its virulent forms as the pathogenic agent of the disease.

Lemoine² in 1895 likewise affirmed his belief that the streptococcus bore an etiological relationship to scarlet fever, and that the point of entrance of the germs was the throat.

Class³ in 1897 described a diplococcus, sometimes appearing in short chains, which he found constantly in the pharynx in scarlatina. It was also found in the blood, but rarely after the first day of the disease. Intravenous injections of this organism in white swine were said to produce an affection closely simulating scarlet fever.

Schamberg and Gildersleeve,⁴ in a bacteriological examination of the throats of 100 cases of scarlet fever, found the diplococcus described by Class in but 15 cases. They found that, while this organism appeared as a large diplococcus when first isolated and cultivated on certain media, it later decreased in size to about 0.6μ , and appeared as a micrococcus, occurring singly and in pairs, with an occasional short chain. The organism reacted upon the various media in a manner similar to the ordinary staphylococci.

In 1900 Baginsky and Sommerfeld⁵ described a streptococcus almost constantly found in the throat and blood of scarlet-fever patients. This organism sometimes appeared in short chains and in pairs. These investigators tentatively regard the streptococcus as the cause of the disease.

Protozoa in Scarlet Fever.—In 1887 L. Pfeiffer⁶ described protozoa-like bodies in the blood of scarlet fever and vaccinia. The significance of these was not explained.

Mallory⁷ recently described certain bodies in the skin in four cases of scarlet fever which he regarded as stages in the developmental cycle of a protozoon. They form a series which are closely analogous to the series seen in the asexual development (schizogony) of the malarial parasite, but in addition there are certain coarsely reticulated forms which may represent stages in sporogony or be due to degeneration of the other forms.

These bodies found in the skin fixed in Zenker's fluid and stained with eosin and methylene blue can be divided into two groups. The first group consists of round, oval, elongated, and lobulated bodies

¹ *La pathogénie de la scarlatine*, Paris, 1895, p. 126.

² *Bull. et mém. Soc. méd. des hôp. de Paris*, 1895 and 1896.

³ *New York Medical Record*, September, 1899, p. 330; *Journal of the American Medical Association*, 1900, vol. xxxiv., No. 34; *ibid.*, 1900, No. 13, p. 799.

⁴ *Transactions of the Philadelphia Pathological Society*; also *Medicine*, September, 1904.

⁵ *Berliner klin. Wochenschrift*, 1900, Nos. 27 and 28, p. 588.

⁶ *Zeitschrift f. Hygiene*, Bd. II., 1887.

⁷ *Protozoon-like Bodies Found in Four Cases of Scarlet Fever*, *Journal of Medical Research*, January, 1904.

from two to seven microns or more in diameter. Most of the bodies seem to be composed of a close-meshed, finely granular reticulum.

The second group of bodies have a striking radiate structure. They are found in vacuoles and in the protoplasm of epithelial cells, and free in the lymph spaces and vessels of the corium just underneath the epidermis. These radiate bodies vary from four to six microns in diameter. They are usually spherical, contain a central round body around which are grouped ten to eighteen narrow segments, which in some cases are united, but in others are sharply separated laterally from each other. Sometimes the segments are free.

Mallory proposes for these bodies the name "*cyclaster scarlatinalis*," in consequence of the frequent wheel and star shapes of the rosettes, its most distinguishing characteristic.

These bodies were found only early in the disease, most abundantly in the skin of a boy who died forty-eight hours after the appearance of the eruption. A number of cases in the desquamative stage of the disease were examined with negative results.

The Relation of the Streptococcus to Scarlet Fever.—The finding of streptococci in scarlet fever by Fränkel and Freudenberg, Babes, Loeffler, Klein, Crookshank, Fiessinger, Dowson, Bergé, Lemoine, and Baginsky and Sommerfeld has already been referred to.

Lemoine, in a study of the throat in 117 cases of scarlet fever, found the streptococcus alone in 93 cases and present with other bacteria in 14 cases.

In 1900 Baginsky and Sommerfeld¹ published the results of a large number of bacteriological examinations in scarlet fever. In 411 cases of this disease streptococci were constantly found in the throat. In a later series of 290 cases streptococci were found in 285. In this group they were found alone 21 times, with staphylococci 222 times, with diplococci 25 times, and with diphtheria organisms in mixed cases 17 times. In 701 cases, therefore, streptococci were absent but 5 times.

Pearce² found streptococci alone or associated with other organisms in scarlet fever, in abscessed ears, in the antra of Highmore, in bronchopneumonia, serofibrinous pleurisy, empyema, acute mitral endocarditis, cervical lymphadenitis, embolic abscesses in the lungs and kidneys, acute pericarditis, acute diphtheritic endometritis, etc. In 11 cases of general infection the streptococcus was found in 9. Streptococci have been found at autopsy in the heart's blood, liver, kidneys, and other organs.

Weaver³ found streptococci in the tonsils of 18 cases. Cultures from the skin of 15 cases disclosed nothing of interest.

Slawyk⁴ in 98 fatal cases found bacteria in the blood of 52; streptococci were found 39 times, and streptococci and staphylococci 6 times.

Hektoen⁵ found streptococci in the blood of scarlet-fever patients,

¹ Berliner klin. Wochenschrift, 1900, Nos. 27 and 28.

² Report of Boston City Hospital, 1899.

³ Journal of the American Medical Association, 1903, vol. v, p. 609.

⁴ Jahrbuch. f. Kinderheilk., 1901.

⁵ Journal of the American Medical Association.

more particularly in the severe cases. They were absent, however, in some of the fatal cases.

Schamberg and Gildersleeve¹ examined, bacteriologically, the throats of 100 patients suffering from scarlet fever. A great variety of organisms was isolated. Streptococci were found in 88 cases and staphylococci in 73. The staphylococci varied in pathogenic power, but, as a rule, killed rabbits and guinea-pigs in a short time.

Cultures were also made from the throats of 100 apparently well persons and from 82 per cent. of them streptococci were obtained. A number of these were tested and found to be as virulent as those from other sources.

The almost constant presence of streptococci in throats of scarlet-fever patients and their activity in the production of such complications as otitis media, cervical abscess, and endocarditis have led certain writers to affirm their belief in the streptococcal origin of scarlet fever. Dowson, Bergé, and Lemoine have, in recent years, particularly championed this view. There can be no question as to the constancy with which the streptococcus is found in scarlet-fever throats, and at autopsy in the various organs and tissues. This would constitute a strong argument in favor of its specific pathogenicity in scarlet fever, were it not for the frequency with which it is found in other infectious diseases. For instance, in smallpox it is scarcely less ubiquitous than in scarlatina.

It is commonly found in the late pustules of smallpox, and in many of the cutaneous complications, such as boils, impetigo, abscesses, erysipelas, gangrene, etc. After death streptococci are found in the cutaneous lesions and internal organs in nearly all cases. There would appear to be in many cases an agonal or post-mortem diffusion of streptococci throughout the tissues. In 40 autopsies on smallpox patients made by Perkins and Pay, streptococci were found distributed throughout the body in 38. Ewing found streptococci in about 90 per cent. of the skin lesions at autopsy; he also noted the presence of streptococci in the blood after death in every one of 29 cases examined.

It is evident from the above and other investigations that the streptococcus is almost constantly found in fatal cases of smallpox. While no one can seriously entertain the idea that its role in smallpox is causal, it is so uniformly present that some writers believe it bears a peculiar relationship to the disease differing from most secondary infections.

Many writers regard the smallpox bacteræmia as the most frequent cause of death in smallpox. Councilman² says: "As a result of the study of the disease, both by culture of the lesions and organs and by microscopic examination of the tissues, we are inclined to regard bacterial infection as a more important agent in bringing about a fatal termination than the specific parasite. . . . The bacteria are

¹ A Bacteriological Study of the Throats of One Hundred Cases of Scarlet Fever, etc. : Transactions of the Philadelphia Pathological Society ; also *Medicine*, September, 1904.

² *Journal of Medical Research*, February, 1904, p. 358.

chiefly streptococci." Perkins and Pay, and likewise Councilman, suggest that the streptococci in smallpox gain entrance to the circulation through the bronchial and pulmonary mucous membrane.

It would seem that the relationship of the streptococcus to scarlet fever and to smallpox is quite similar. It gives rise in both to numerous complications and not infrequently leads to a fatal termination. The proof that it is not the cause of smallpox is easy of demonstration; the proposition that the streptococcus bears no etiological relationship to scarlatina is more difficult to disprove.

It appears to us reasonable that in certain infectious diseases, particularly scarlatina and smallpox, the resisting powers of the tissues are so weakened against the streptococcus, that this organism invades the system and works its noxious effects.

Until the streptococcus found in scarlet fever is shown to possess properties which trenchantly distinguish it from other streptococci, and until this disease is experimentally produced by inoculation of a pure culture of such an organism, the belief in the causal relationship of the streptococcus to scarlet fever cannot be maintained.

THE PATHOLOGY OF SCARLET FEVER.

The Blood.—The older writers contented themselves with a description of the fluidity, coagulability, and color of the blood. At the present day accurate methods are in use which throw considerable light upon the changes in the circulating fluid.

Felsenthal and Bernard, from a study of the specific gravity of the blood, conclude that it is reduced in all cases of scarlet fever. The reduction in hæmoglobin is disproportionately great as compared with that of the specific gravity.

Hayem was one of the first writers to point out a reduction in the red blood corpuscles and an increase of the leukocytes. He also called attention to the frequent increase of fibrin, especially in attacks accompanied by bad throats and suppurative complications.

Ewing¹ states that the gradual loss of red cells noted by Hayem has been fully verified by Kotschetkoff, who found a reduction to three millions or less in nearly every case. Zoppert, on the other hand, found more than four million corpuscles in 5 out of 6 cases. A number of other observers have also found in a considerable number of cases but a slight decrease of the red cells.

Estimations of the *hæmoglobin* percentage were made by Widowitz² in 14 cases of scarlet fever. In all but 1 the hæmoglobin was strikingly high in the beginning, then falling until the commencement of convalescence, when it again increased in quantity. When nephritis develops a more decided fall takes place.

¹ Clinical Pathology of the Blood, 1901.

² Hämoglobingehalt des Blutes Gesunder und Krankerkinder; Jahrbuch f. Kinderh., N. F. xxviii. p. 384.

Leukocytes.—The white cells have been carefully studied by a number of investigators, notably Kotschetkoff and Bowie. There is general agreement as to the uniform and early appearance of leukocytosis.

Kotschetkoff¹ states that leukocytosis is influenced by the type of the disease; mild cases show usually from 10,000 to 20,000 white cells; moderately severe cases, from 20,000 to 30,000 cells; and the severe and usually fatal cases from 30,000 to 40,000 cells; in some rapidly fatal cases over 40,000 leukocytes were present. Yet Rieder's² cases seldom gave more than 20,000 cells, although some were complicated and fatal. Felsenthal³ found in six attacks of moderate severity in children from 18,000 to 30,000 leukocytes.

Bowie⁴ gives the results of the careful and repeated examination of 167 cases. He concludes that (1) practically all cases of scarlet fever show leukocytosis; (2) the leukocytosis begins in the incubation period, very shortly after infection; it reaches its maximum at or shortly after the acme of the disease and then gradually diminishes to normal; (3) in simple uncomplicated cases the maximum is reached during the first week, and the normal generally some time during the first three weeks; (4) the more severe the case, the higher is the leukocytosis and the longer it lasts; the milder the case, the slighter the leukocytosis and the shorter time it lasts; (5) a favorable case of any variety of the disease has always a higher leukocytosis than an unfavorable one of the same variety; (6) the temperature has no effect on the leukocytosis. These observations are in complete accord with those of Kotschetkoff.

DIFFERENTIATION OF LEUKOCYTES.—Bowie states that the polymorphonuclear leukocytes are increased relatively and absolutely at first, and then fall to normal; the lymphocytes act in an inverse manner. In simple cases this cycle occurs within the course of three weeks. Kotschetkoff estimates the number of the polymorphonuclears as varying between 85 per cent. and 98 per cent., according to the severity of the disease; the highest point is reached on the second day of the eruption, a gradual diminution then occurring. The lymphocytes are at first diminished, but later increase to normal.

According to Bowie, the eosinophiles are diminished at the onset of the fever. In simple favorable cases a rapid increase then occurs until the height of the disease is passed, when a gradual decline to normal takes place, the latter occurring after the disappearance of the leukocytosis.

The more severe the case the longer are the eosinophiles subnormal before they rise again. In fatal cases they never rise, but sink rapidly toward zero. Kotschetkoff says that eosinophiles in all but severe cases are normal or subnormal at first; after two or three days they steadily increase, reaching a maximum of 8 per cent. to 15 per cent. in the second or third week, and then decline slowly to normal about

¹ Quoted by Ewing, loc. cit.

² Quoted by Ewing.

³ Quoted by Ewing.

⁴ Leukocytosis in Scarlet Fever, *Journal of Pathology and Bacteriology*, March, 1902.

the sixth week. The eosinophiles may disappear early in the disease in cases which prove fatal.

While the above quoted results of Kotschetkoff and Bowie are in striking harmony, certain other observers have noted divergent findings. Sevestre,¹ from an examination of 13 cases, concluded that "in severe cases it was found that the percentage of the finely granular eosinophiles was always high," and "in the majority of cases examined the percentage of the coarsely granular eosinophiles was found to be diminished during the whole period of the disease."

Ewing says that Weiss found no eosinophiles in 1 case at the height of the exanthem, and Rille observed marked eosinophilia in a fatal case; Bensaude observed as high as 20 per cent. of eosinophiles in one instance.

INFLUENCE OF TEMPERATURE, RASH, AND COMPLICATIONS.—Kotschetkoff states that the grade of the leukocytosis depends upon the severity of the disease, especially the angina, but not upon the height of the temperature. Complications such as lymphadenitis, otitis, and nephritis usually have little effect on the leukocytosis.

According to Bowie, the temperature has no effect on the leukocytosis. In complications, the leukocytes go through a cycle of events similar in all respects to that of the primary fever as regards both sum-total and differential leukocytosis, and the same laws govern the behavior of the leukocytes in both cases.

Sevestre says that "complications such as otorrhœa, rhinorrhœa, and adenitis tend to increase the number of white cells." He also states that a relationship exists between the leukocytosis and the rash; the former varies with the severity of the latter, and with the fading of the same the leukocytes show a marked diminution in number.

Rieder and Turk² have noted a high persistent leukocytosis, especially in those cases followed by nephritis or other complications. Pee³ found an increase in the leukocytes in 2 cases during a late adenitis.

Bowie believes that the simple counting of the leukocytes is of but little *diagnostic* value. A differential count may, however, be of aid, for scarlet fever is one of the few acute infections in which one finds an early increase of the eosinophile cells and a persistence of the increase for some time.

As regards *prognosis* he says: "In simple, severe scarlatina, if the leukocytosis be high and rising, a favorable course may be predicted; if it be low and stationary a tedious course may be expected. If the eosinophiles show a relative increase the augury is good; if they are normal or subnormal after the first day or two, then, in all probability, the case will be severe. The persistence of a relative increase of the eosinophiles suggests some complication, whereas, if they come down to normal in the usual manner, one may be free from anxiety as regards complications."

¹ St. Bartholomew's Hospital Reports, 1896, vol. xxii, p. 225 et seq.

² Quoted by Ewing.

³ Quoted by Ewing.

MORBID ANATOMY OF SCARLET FEVER.

But little information is obtained by post-mortem examination in uncomplicated cases of scarlet fever that cannot be foretold by the symptomatology of the disease. The gross morbid changes are usually observed in the skin, tongue, throat, and lymphatic structures of the body. Indeed, the most uniform gross alteration is a hyperplasia of all of the lymphoid structures of the body.

After death the eruption commonly fades away completely except in those cases in which the rash has been intense. In the hemorrhagic forms the petechial spots will, of course, remain visible.

Histological Changes in the Skin.—The skin has been studied by a number of investigators, but principally by Klein, Unna, and Pearce.

Klein¹ studied the changes in the skin in 20 cases. He found the epidermis slightly thickened, particularly the mucous layer. Many of the rete cells showed dividing nuclei. Between the horny and mucous strata were small spaces containing granules resembling micrococci.

In the rete Malpighii were found lymph corpuscles with deeply staining nuclei. In the corium the epithelial cells of the follicles and sweat glands exhibited an increase of the nuclei. The bloodvessels were distended by corpuscles and occasionally by fibrin. The nuclei of the lymphatics and of the endothelial and muscular coats of the arteries were increased.

Neumann² noted swelling of the rete cells and elongation of the prickle cells, between which was evident a cell infiltration, occasionally containing red blood corpuscles. The bloodvessels and lymphatics were dilated. There was slight cellular proliferation around the sweat glands, hair follicles, and bloodvessels.

Kaposi³ regards the changes in the skin as the result of vascular congestion with moderate cell infiltration; the papules and vesicles occasionally seen are due to an excessive exudation and cell proliferation in the papillæ and in the rete mucosum.

Unna⁴ examined the skin of 7 cases of scarlet fever. His findings are briefly as follows: There is a marked wrinkling of the whole epidermis along with the papillary body, which is due to an overstretching of the epidermis by the sodden, engorged cutis and to subsequent distortion, after excision of the skin, when the cutis contracts. The elasticity of the cutis indicates that during life it could not have been the seat of œdema.

The bloodvessels of the true skin are enormously dilated, suggesting almost distention by artificial injection. This distention, which is present even after death, is the result of a *vascular paralysis*. White blood corpuscles are extremely scant, scarcely more than is found under normal conditions.

¹ Local Government Report, viii. 24, London, 1876; quoted by Pearce, loc. cit.

² Med. Jahrbücher, 1882, p. 152.

³ Path. und Therapie der Hautkr., Vienna, 1899, p. 243.

⁴ Loc. cit., p. 629.

No particular changes are found, at the height of the eruption, in the prickle layer. There is absence of mitosis, oedema, and of any dilatation of the interepithelial lymph spaces. Mitoses are found first and pretty numerous in the stage of desquamation.

In view of the above findings, Unna regards the changes in the scarlet fever skin as paralytic and not inflammatory.

Pearce¹ examined the skin in 8 cases between the second and sixteenth days, and 1 on the thirty-second day.

On the second day, beyond a congestion of the bloodvessels and slight dilatation of the lymphatics, no changes were observed. In 3 cases examined on the third day, a few leukocytes and lymphoid cells were seen in and grouped around smaller lymphatics beneath the rete Malpighii. From the fifth to tenth days the most marked condition was an infiltration of the epithelium with polymorphonuclear leukocytes. The cells apparently leave the bloodvessels beneath the rete and pass up between the epithelial cells and collect in the superficial layers of dead cells, with which they are thrown off. In the connective tissue beneath the epithelium were numerous polynuclear leukocytes and a few plasma cells. The lymphatics were widely dilated and contained many leukocytes. By the twelfth and sixteenth days the leukocytic infiltration had nearly disappeared. In a late desquamating case the rete contained numerous mitotic figures.

Tongue.—When death occurs early in the course of the disease the enlarged papillæ may be visible at post-mortem. Pearce² made a microscopic study of the tongue in 8 cases, all between the second and ninth days.

The process in the tongue is said to be similar to that in the skin, but is more marked and begins earlier. The chief changes consist of a dilatation of the papillary bloodvessels and lymphatics, a leukocytic infiltration of the epithelial layers, particularly pronounced over the papillæ, and the presence of leukocytes in and around the bloodvessels. The polymorphonuclear leukocytes wander between the epithelial cells, collect beneath the superficial epithelium, with which they are cast off. The most pronounced cell infiltration is seen between the fourth and ninth days. Mast-cells are increased in number and plasma cells are seen in small numbers about the bloodvessels. Mitoses in the epithelial cells are frequent. Pearce regards the process as inflammatory and suggests that the exciting cause of the leukocytic infiltration may be a positive chemotaxis excited by the presence in the tissues of the scarlet-fever toxin, or by substances formed by its action on the superficial epithelial cells.

Lymphatic System.—In 1872 Harley³ studied the post-mortem changes in 28 cases of scarlet fever and concluded that it was a disease of the lymphatic system characterized by hyperplasia of the lymph glands, spleen, tonsils, liver, and other lymphatic structures of the

¹ Scarlet Fever, its Bacteriology and Gross and Minute Anatomy, Medical and Surgical Reports of Boston City Hospital, 1899.

² Loc. cit.

³ Med. Chir. Trans., London, 1872, lx. p. 102.

body. He, therefore, proposed to substitute for the name scarlet fever the term lymphatic fever.

There can be no doubt that pronounced hyperplasia of the lymphoid tissues is a constant and conspicuous accompaniment of scarlet fever.

Pearce¹ found the mesenteric, retroperitoneal, bronchial, and tracheal glands enlarged in all cases. The superficial lymph nodes, such as the cervical, axillary, and inguinal, were also found enlarged. The glands were quite firm, and, on section, pale and watery.

Klein and Pearce have both made histological studies of the glands. Klein² examined the lymph glands in 8 cases. The centres of the glands were transparent and composed of large cells resembling giant cells. There were also large cells with transparent vesicular nuclei. In the sinuses were small cells and also large granular cells, with one or two transparent nuclei (endothelial).

Pearce studied the glands, including the mesenteric, cervical, and bronchial, in 20 cases. The changes observed were similar to those seen in the spleen, but were not present in all cases. The bloodvessels were congested, and in 3 cases small hemorrhages were seen. The lymph sinuses were dilated and contained many large endothelial cells lying loose in their lumina. These cells were frequently observed to be phagocytic, containing a number of disintegrated lymphoid cells. Plasma cells, exhibiting numerous mitotic figures, were found throughout the lymph nodes.

Spleen.—The gross appearance of the spleen, according to Pearce, permits of a classification into two different groups. There is no increase in pulp, but a marked enlargement of the Malpighian bodies. In such cases the spleen is firm, and the capsule smooth but not tense; on section there is seen a dark-reddish background, dotted everywhere with regularly or irregularly enlarged Malpighian bodies. This condition was noted in 13 out of 23 cases examined.

In the other class the splenic pulp is greatly increased and the Malpighian bodies indistinct. The spleen is then large and soft. This condition was seen in 7 cases, in 2 of which, however, there was enlargement of the Malpighian bodies. In the remaining 3 cases absolutely no change in the gross appearance of the spleen was visible. The differences described do not seem to depend upon the age of the patient, the stage of the disease, nor the intensity of the infection.

Klein³ noted, in 8 cases examined histologically, an enlargement of the Malpighian bodies. A peculiar pale area, composed of endothelial-like cells, was observed in the centre of the bodies. The intima of the bloodvessels exhibited a hyaline degeneration, at times leading to obliteration of the lumen.

Pearce made a careful histological study of the spleen in 21 cases. The enlargement of the Malpighian bodies was found to be due to a central massing of large endothelial cells in addition to the presence of numerous plasma cells. These were abundantly present also around

¹ Loc. cit.

² Transactions of the Pathological Society of London, 1877; quoted by Pearce.

³ Quoted by Pearce.

the bloodvessels, in the lymphatics, and along the trabeculae. The bloodvessels were greatly congested. A peculiar condition noted was a collection of cells, chiefly plasma and lymphoid cells, but occasionally also a few leukocytes, beneath the endothelial lining of the vessels.

Liver.—The gross changes in the liver are not pronounced. It exhibits usually, although by no means constantly, some degree of enlargement. The consistence is ordinarily less firm than the normal liver. In 1 case Pearce noted on the surface a number of minute, yellowish areas, which were shown to represent necrotic foci. Roger observed in 2 cases a number of scattered red spots due to subcapsular ecchymosis, a sort of purpura of the liver.

Histologically, the changes in the liver are those of an acute febrile infectious disease. In 22 cases examined by Pearce the liver cells in each instance exhibited the degenerative changes common to fevers. In 4 cases distinct fatty degeneration was noted, and in 7 cases extensive fatty infiltration. An infiltration of lymphoid cells with a few polymorphonuclear leukocytes was found around the portal vessels in 11 cases. A few eosinophiles and plasma cells were seen, the latter more particularly in the bloodvessels. Phagocytic endothelial cells were found in the bloodvessels in 5 cases. Focal necrosis of the liver was observed in 4 cases. The focal areas seemed to arise from endothelial cells, derived in part from the capillary endothelium of the liver, and, in part, from embolism through the portal circulation of cells originating in the spleen. The changes are similar to those described by Mallory as frequently occurring in the liver in typhoid fever.

Roger and Garnier¹ made histological examinations of the liver in 12 cases. The changes described by them are of different types: one series concerns the mesodermic elements of the liver—leukocytic infiltration, thickening of the capsule of Glisson, etc., inflammation of the vessels; the other affects the epithelial tissue. The first stage of inflammation in the liver is leukocytic infiltration of the portal spaces. Later, the epithelial cells are altered; they may merely show unequal coloration of the nuclei or they may degenerate in considerable number around the portal spaces, or, finally, a number only may degenerate, forming a limited focus which may subsequently become infiltrated with leukocytes. At the same time inflammation of the conjunctive tissues may increase and the cells present may undergo hyaline and fatty degeneration or fatty infiltration. When parenchymatous hepatitis is extensive the interstitial changes also become pronounced.

Gastrointestinal Tract.—The mucous membrane of the pharynx, tonsils, and soft palate show, under the microscope, the usual changes observed in inflammation of these structures.

Fenwick² described changes in the mucous membrane of the *stomach* analogous to the desquamation of the cutaneous surface; in severe cases there was an absolute loss of epithelium. In addition he found a

¹ Des modifications anatom. et chimiq. du fofe dans la scarlatine, *Rev. de m d.*, March 10, 1900, and Roger, *Les maladies Infect.*, p. 1066.

² *Medico-Chir. Trans. of London*, 1862, xlvii.

dilatation of the bloodvessels and a filling up of the gastric tubules with a granular and fatty material and small cells.

Crooke, in a study of 6 cases, found catarrhal gastritis in all, and, in the severe cases, interstitial and follicular gastritis characterized by hyperplasia and necrosis of the lymph follicles, and infiltration of the muscular coat with round cells. Hesselwarth found 21 instances of severe gastroenteritis among 81 autopsies.

Pearce examined the stomach histologically in 6 cases. In a case dying upon the second day the surface of the stomach was covered with a thick layer of mucus and necrotic epithelial cells, containing numerous leukocytes and cocci. Polymorphonuclear leukocytes and granular material were found in the tubular glands, and numerous plasma cells between the tubules. Enlarged and altered lymph nodules were seen in the lower part of the mucous membrane; 4 other cases showed similar but less-marked changes.

The *intestines* exhibit changes very similar to those seen in the stomach. Virchow described marked hyperplasia and swelling of the lymph follicles. Crooke says that Peyer's patches at times look like those found in typhoid fever during the first week.

Bone-marrow.—Pearce¹ examined the bone-marrow in 11 cases, of which 2 were adults. In all the cases the bone-marrow was very cellular. Giant cells and nucleated erythrocytes were seen and eosinophile cells were found in abundance. Lymphoid cells and neutrophilic leukocytes were present in fair numbers. The principal cells, however, seen in all cases were about the size of and closely resembled the plasma cell. They formed the bulk of the cells found in the bone-marrow.

Roger² found the bone-marrow absolutely normal in 1 case, and in another evidence of slight reaction of the medullary tissue.

Heart.—The cardiac muscle suffers in scarlet fever from two chief causes—the scarlatinal poison and, secondarily, from involvement of the kidneys. The most common changes observed are cloudy swelling and fatty degeneration, processes which are observed in many infectious diseases.

Romberg³ has pointed out that the interstitial connective tissue, as well as the myocardial tissue, shows pathological alteration. The muscle fibres are separated by masses of cells and the arterial bloodvessels exhibit distinct inflammatory changes.

Pearce, in an examination of 9 cases, demonstrated fatty degeneration in 5. Segmentation and fragmentation of the myocardium were observed in a few instances.

The above changes doubtless result from the poison of the disease. The heart frequently undergoes hypertrophy and dilatation as a result of a coexisting nephritis.

Friedländer⁴ states that in children with nephritis the heart increases

¹ Loc. cit.

² Loc. cit.

³ Ueber die Erkrankungen des Herzmuskels bei Typhus abdom., Scharlach und Diphtheria; Deutsch. Archiv f. klin. Med., Bd. xlviii. and xlix.

⁴ Ueber Herzhypertrophie; Du Bois-Reymond, Archiv f. Physiolog., 1891.

in weight on an average about 40 per cent. Jüger is of the opinion that two-thirds of all cases of scarlatinal nephritis are accompanied by cardiac *hypertrophy* and often by *dilatation*. When the integrity of the heart muscle is compromised in the earlier days of the disease by the fever and the scarlatinal poison, it becomes unable to withstand the increased pressure later when the kidneys become involved, and thus undergoes dilatation. Silberman¹ explains the heart changes as follows: (1) there is no disease in which the elimination of water is so suddenly and enormously diminished as in scarlatinal nephritis; (2) the glomeruli are principally affected; (3) there is extensive involvement of the kidney structure; (4) the oedema compresses the blood-vessels of the skin and in this way increases heart pressure; (5) increased resistance in the aortic system is more readily followed by cardiac hypertrophy in children than in adults.

Riegel² states that increased arterial tension accompanies all cases of scarlatinal nephritis, and as a result thereof *hypertrophy* of the heart takes place. The enlargement is sometimes observed a few days after the development of the nephritis. Forchheimer believes that from the effects of the scarlatinal toxin dilatation commonly takes place, even if lasting only a short time, with hypertrophy following as compensatory.

A clinically demonstrable *pericarditis* is distinctly uncommon in scarlet fever. Slight grades of pericardial inflammation are occasionally seen at autopsy. When nephritis is present effusion of serum often occurs, in some cases giving rise to enormous distention of the pericardial sac. When inflammation is present the exudate may be sero-fibrinous or purulent; in the latter event streptococci and staphylococci are usually found upon culture.

Endocarditis.—Endocarditis of the cardiac wall is said by von Jürgensen,³ to be more common than valvular endocarditis. Forchheimer considers endocarditis as a very common complication of scarlet fever. The margins of the valvular segments are, in mild cases, the seat of small excrescences, in severe cases larger ones constituting a verrucous endocarditis.

Roger in 2213 personal examinations, of which 1727 were in adults, observed endocarditis but twice, while extracardiac murmurs were found 692 times. In 1 of the cases of endocarditis there were ulcerovegetating lesions and an abscess of the myocardium. The streptococcus was found to be the cause of the abscess.

Antra of Highmore.—Pearce found an inflammation of these cavities in 3 cases. In 2 both cavities were filled with an abundant purulent fluid, and the process was a true empyema. In both of these cases both middle ears were infected, and in one of them the sphenoidal sinus was filled with a greenish-yellow pus.

¹ Jahrbuch f. Kinderheilk., N. F., 1894, xxxvii.; quoted by Forchheimer, loc. cit.

² Ueber die Veränderungen des Herzens u. des Gefäßsystems bei Acuter Nephritis; Zeitschr. f. klin. Med., 1884, Bd. vii.

³ Loc. cit.

Pulmonary Complication.—In a series of 23 autopsies Pearce found *bronchopneumonia* in 8 cases, usually in the form of small, discrete nodules, scattered along the back or base of the lung. In 2 cases the process was confluent, involving the greater portion of one or more lobules. In 5 of these cases both the streptococcus and the staphylococcus aureus were found. In 1 case the latter was found associated with the pneumococcus; in 1 case the streptococcus was found alone.

A *serofibrinous pleurisy* was noted in 1 case as the result of streptococcus infection, and in another an empyema with atelectasis of the lung. In the latter a small abscess cavity was found on the surface of the lung.

Kidneys.—A voluminous and somewhat confusing literature has accumulated upon the subject of scarlatinal nephritis.

Klebs, in 1876, was one of the earliest writers to call attention to a glomerulonephritis occurring during convalescence from scarlet fever. He divided the kidney alterations into three groups: (1) a granular desquamation of the epithelium in the febrile stage; (2) an interstitial nephritis frequently seen late in the disease; the kidney in this condition is large, lax, smooth on section and shows grayish-white nodules; (3) a glomerulonephritis during convalescence.

In 1883, Friedländer, from a careful study of the kidney in 229 autopsies, divided scarlatinal nephritis into three classes: (1) an early catarrhal nephritis, occurring during the first week; (2) an interstitial nephritis in which the kidney is large, white, and hemorrhagic; this form occurs in severe cases with bad throats and other septic complications; and (3) an acute glomerulonephritis which develops during convalescence. The latter condition occurred in 42 cases and was regarded by Friedländer as the most characteristic kidney lesion of scarlet fever. In this condition the interstitial tissue is practically normal, the glomeruli being solely involved.

Councilman in 1897 characterized the condition of the kidney in 3 cases of scarlet fever as a pure interstitial nephritis. He states that glomerular nephritis occurs chiefly in measles, acute endocarditis and diphtheria, and acute non-suppurative interstitial nephritis in diphtheria and scarlet fever. In the latter disease the kidney is large, pale, and mottled. The principal lesion is an acute cellular infiltration with a few phagocytic endothelial cells and leukocytes. The origin of the plasma cells is presumed to be lymphoid cells which have undergone conversion in the spleen, and which emigrate from the bloodvessels and undergo mitotic change in the kidneys.

Pearce,¹ in a study of 23 cases, found degenerative changes in all. Of 8 specimens examined in the fresh state, 6 showed a more or less marked fatty degeneration. *Acute interstitial nephritis* was the most important lesion present. In 4 cases this process was extensive and in 5 slight. In the former the cellular infiltration was most marked in the cortex just beneath the capsule, around the glomeruli and around

¹ Loc. cit.

the bloodvessels in the intermediate zone. The cellular areas were made chiefly of plasma cells with a few lymphoid cells and leukocytes. *The glomeruli were unaffected.* These cases were fatal on the eighth, ninth, fourteenth, and fifteenth days respectively.

From the writings of various authors it is seen that a considerable difference of opinion exists as to the most characteristic kidney changes in scarlet fever. Councilman expresses the view that differences in local resistance doubtless influence the susceptibility of the various structures. He believes that in all serious lesions of the kidneys the changes in some cases may be principally in the glomeruli, and in others in the interstitial connective tissue. The glomerular lesions may be accompanied by degenerative alterations in the epithelium of the tubules, which may or may not be secondary. Hyperplasia of the connective tissue cannot be regarded as secondary to tubular changes.

Certain investigators, particularly Marie, Haskine, Guinon, and Babes have found streptococci in nearly all forms of scarlatinal nephritis. How far the inflammatory changes are due to such micro-organisms and to what extent the scarlatinal toxin is responsible, time and future research must determine.

CHAPTER VIII.

SCARLET FEVER (*Continued*).

THE DIAGNOSIS OF SCARLET FEVER.

WHEN scarlet fever exhibits itself in a pronounced and typical form the diagnosis is very simple. As is the case with all diseases, however, aberrant and unusual cases quite frequently present themselves, in which circumstance the establishing of the nature of the disease offers the most perplexing difficulties.

We are of the belief that more errors of diagnosis are made in connection with scarlet fever than with any other acute disease. On the one hand, many cases of extremely mild scarlet fever are overlooked, and, on the other hand, rashes from other causes resembling that of scarlatina are not infrequently diagnosed as the latter disease.

It should be remembered that there is no one symptom of scarlatina which is pathognomonic of the disease. The rash, the most conspicuous symptom and the one which has given the affection its name, is not in itself characteristic, inasmuch as an almost identical exanthem may occur in other conditions. Nor does its absence entirely exclude the diagnosis of scarlet fever. Indeed, we may have a scarlet fever without eruption, *scarlatina sine eruptione*; without fever, *scarlatina sine febre*; or without sore throat, *scarlatina sine angina*.

When all of the symptoms of scarlet fever are developed an unmistakable syndrome is presented. Who could fail to diagnose a disease characterized by sudden vomiting, high fever, prostration, diffuse punctiform rash, circumoral pallor, red and swollen throat, enlarged glands, strawberry tongue, followed by desquamation and albuminuria? But, unfortunately, this picture is often incomplete. Those who have had experience with scarlet fever have observed that in severe cases the various symptoms are usually well pronounced, whereas in mild cases all of the symptoms are commonly poorly marked. When the eruption is intense the throat is usually severely attacked, the tongue is characteristic, and the fever is high. When, on the other hand, the general symptoms are very mild the rash is, as a rule, faint or poorly developed. It is under the latter circumstances that the diagnosis becomes so difficult, for the complex of symptoms upon which the foundation of the diagnosis rests is too weak to support it.

How often do we see cases in which the rash is faint, the constitutional symptoms mild, and the throat and tongue uncharacteristic! The evidence appears very slender upon which to base the diagnosis of a disease which necessitates two or more months of isolation. Under these circumstances the physician will do best to postpone the pro-

nouncement of a diagnosis until the further course of the disease is watched. *In some cases it remains impossible to be sure of the scarlatinous nature of the disease.*

Etiological Evidence.—The diagnosis in cases of scarlet fever with obscure symptoms is often simplified by the discovery of the disease in a person to whom the patient has been exposed. In institutions for children the existence of an epidemic often clarifies an individual diagnosis which would be quite impossible to make under other circumstances. Close enquiry and examination will sometimes discover a desquamating and hitherto unrecognized case of scarlet fever to be the origin of an institution epidemic.

The diagnosis of scarlet fever in doubtful cases is sometimes confirmed by the disease being transmitted by the suspected patient to another person.

Diagnostic Value of the So-called Strawberry Tongue.—In the very beginning the tongue in scarlet fever is heavily coated with a whitish fur through which scattered red papillæ are frequently visible. In about forty-eight hours the coating peels off and there is seen a red tongue studded with enlarged papillæ. This condition of the tongue is certainly a symptom of considerable diagnostic importance, and its presence or absence in doubtful cases should be determined and considered in formulating the diagnosis. But several sources of error must be kept in view. In mild cases of scarlet fever in which the rash and general symptoms leave doubt as to the nature of the disease the tongue often fails to present its characteristic appearance. We cannot agree with McCollom, of Boston, who says that the enlargement of the papillæ is present in every case of scarlet fever, if carefully looked for. We have certainly seen a number of children in scarlet-fever wards whose tongues have been quite normal in appearance. Most of these children had mild attacks.

On the other hand, the tongue in well persons shows a variable amount of prominence of the lingual papillæ. We have examined the tongues of a large number of people with a view of determining this point. Anyone who repeats this experience may satisfy himself that the tongue under normal conditions exhibits wide variations in the size and prominence of the papillæ. Moreover, there are certain chronic forms of superficial glossitis in which the papillæ are quite large.

It must be remembered, too, that the most typical strawberry tongue may, in rare cases, occur in affections other than scarlet fever. In a few severe cases of scarlatiniform erythema, occurring during the course of smallpox, we noted very distinct "strawberry" tongues.

However, these exceptions do not invalidate the force of the statement that the presence of pronounced enlargement of the lingual papillæ in cases suspected of being scarlet fever is strong confirmatory evidence. The negative value of the absence of the characteristic tongue is of less importance.

The Diagnostic Value of Desquamation.—The statement is sometimes made that the occurrence of desquamation after a scarlatiniform

eruption proves the scarlatinal nature of the preceding exanthem. Those who have observed cases of scarlatiniform erythema of the desquamative type recognize the fact that exfoliation of the epidermis is not a phenomenon peculiar to scarlet fever (Figs. 77 and 78).

It is a mistake to regard every diffuse rash that desquamates as scarlet fever. The eruption of scarlet fever is, in all probability, of toxic origin; there are other toxins which appear to be capable of exciting rashes which resemble that of scarlatina. Scaling is the terminal stage of certain pathological alterations in the skin, and the changes in the skin in scarlatiniform erythema are much the same as those occurring in scarlet fever.

The scaling in certain cases of desquamative scarlatiniform erythema is much more extensive than occurs ordinarily in scarlet fever. The occurrence of well-marked lamellar desquamation has more significance, therefore, in differentiating scarlet fever from other affections than from these exfoliating erythemata.

It may be true that the amount of scaling in a rash of given intensity is more pronounced in scarlet fever than in most rashes which simulate it; but exception must be made of desquamative scarlatiniform erythema, which not infrequently causes an exfoliation of the skin in large areas, leading, upon the palms and soles, to the throwing off of the epidermis *en masse*. This occurs in comparatively few cases in scarlet fever.

Too much importance has been attached to the mere occurrence of desquamation in scarlet fever; the time of the onset of scaling, its mode of progression, and its persistence are of more diagnostic importance.

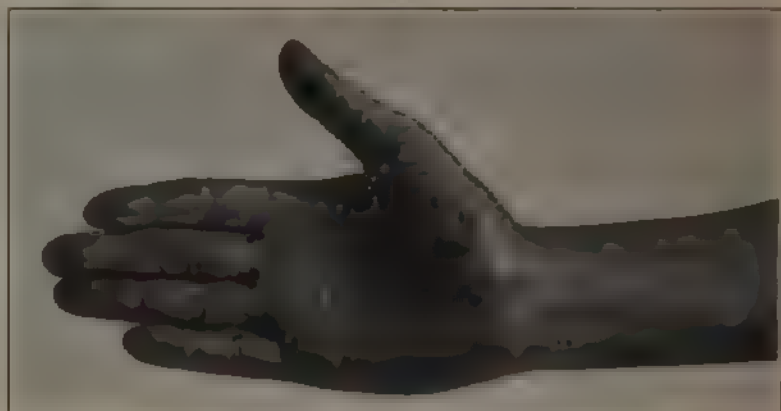
Desquamation in scarlet fever is usually observed first upon the face; this is often seen from the fourth to the sixth day; about the sixth day the same process is noted upon the neck and upper portion of the chest. The hands ordinarily begin to desquamate from the twelfth to the fourteenth day. Upon the feet scaling may not commence until the third week.

Scarlatinoid eruptions, in our experience, begin to scale more quickly, particularly upon the hands and feet. We have seen a well-marked scarlatiniform eruption occurring in smallpox lead to exfoliation of large pieces of the palmar and plantar epidermis on the sixth day. We believe, also, that scarlet-fever scaling persists longer than the scaling after scarlatinoid rashes. We should not insist upon the correctness of this observation, however, as scarlet-fever patients are scrutinized more closely and for a longer period than the non-scarlatinal cases; minute desquamation would thus be detected for a long time in scarlet fever and overlooked, perhaps, in other conditions.

A form of scaling which is commonly seen in scarlet fever is that which begins just beneath the free border of the finger-nails, extending thence down the fingers and exposing to view the new pink epidermis beneath. This appearance is so frequently present as to be suggestive of the disease.

Among the affections which are to be distinguished from scarlet fever the most important are those grouped under the designation of *erythema scarlatiniforme* or *scarlatinoides*.

FIG. 77



Desquamation indistinguishable from that of scarlatina, following a scarlatinoid erythema occurring during the course of smallpox.

FIG. 78



Desquamation in a recurrent scarlatinoid erythema closely resembling that of scarlet fever. This patient has had two attacks almost every year for twenty-five years.

This affection, if it may be called such, is characterized by an eruption which may be quite indistinguishable from that of true scarlet fever. It may be diffused over the entire cutaneous surface and may be punctiform. It is often sudden in its onset and may be attended with malaise and moderate rise of temperature (100° to 102° F.). Occasionally the initial pyrexia is higher, but under such circumstances it soon declines. The throat may be reddened, but there is no swelling of the tonsils and usually no complaint of sore throat.

The eruption has about the same duration as that of scarlet fever, although it is often briefer. It is followed by a desquamation which is ordinarily branny, but which may take place in large flakes.

Desquamative scarlatiniform erythema, termed by some writers *acute exfoliative dermatitis*, differs from the above type in degree rather than in kind.

It is characterized by the appearance of an extensive, often punctiform erythema, which rapidly covers the entire body and is accompanied by more or less febrile disturbance. In the course of three or four days the skin begins to desquamate profusely, being thrown off in large lamellæ or sheets. Epidermal casts of the palms and soles, looking not unlike gloves or slippers, may be exfoliated. The nails may be lost and, in severe cases, the hair also. Before the skin has returned to its normal condition a relapse may occur characterized by fever, erythema, and a second desquamation. In some cases three or four such relapses may take place.

This type of the disease is peculiarly prone to *recurrences*, which may appear every six months or a year. Sometimes marked periodicity is exhibited, the recurrent attacks developing with almost calendar precision. Doubtless many of the cases of scarlet fever recorded in the literature of the subject which are alleged to have recurred five, six, or more times were in reality cases of scarlatiniform erythema of the desquamative type.

These eruptions are due to toxic or septic states or to the action of drugs or sera. Simple scarlatiniform erythema may occur during the course of various infectious processes, such as rheumatism, septicæmia (puerperal or other forms), pyæmia, malaria, typhoid fever, etc. An evanescent scarlatiniform rash may appear before the true exanthem of measles, varicella, smallpox, and vaccinia.

All grades of scarlatiniform erythema may develop during the stage of decrustation of smallpox.

Diphtheria antitoxin and other sera may produce scarlatiniform rashes. Antitoxin rashes developing in the course of diphtheria may, in some cases, so closely simulate the eruption of scarlet fever as to defy all efforts at satisfactory differentiation. Northrup¹ very truly says: "Antitoxin rashes are, at times, most difficult to differentiate from scarlet-fever rashes.

"At the Willard Parker Hospital in New York, where both diphtheria

¹ Addenda to von Jürgensen's article on Scarlet Fever, Nothnagel's Encyclopedia of Practical Medicine, American edition.

and scarlet fever are cared for, it has been almost beyond the power of experts to pronounce definitely upon certain cases."

Intestinal autointoxication may give rise to a scarlatiniform eruption. Crocker says this may follow the use of enemata, which sometimes facilitate the solution and absorption of toxins.

The drugs which most commonly give rise to scarlatiniform eruptions are quinine, mercury, belladonna, and salicylic acid. Many other medicaments occasionally produce scarlatinoid rashes in susceptible subjects. The eruption resulting from the administration of quinine is the most frequent and the most likely to be confounded with scarlet fever. It may be followed by well-marked desquamation.

It is often a matter of great difficulty to differentiate scarlatiniform erythema from true scarlet fever. In the former the invasive symptoms are often extremely mild; the patient commonly does not complain of feeling ill; the temperature elevation is slight, perhaps 101° or 102° F. The throat may be reddened, but the tonsils and uvula are not swollen and exudate is not present upon the tonsils.

The reddened, papillated tongue is, as a rule, absent. The eruption may begin upon any portion of the body; it may be patchy and irregular, or it may be diffuse, with or without punctuation. The glands at the angles of the jaws are not apt to exhibit any pronounced enlargement; albuminuria is rare and otitis media does not occur.

It is thus seen that scarlatiniform erythema may be readily distinguished from a well-pronounced attack of scarlet fever; but the fact must not be overlooked that there are many mild cases of scarlet fever in which the fever is slight, the eruption poorly marked, and the other symptoms correspondingly uncharacteristic.

The significant feature in scarlatiniform erythema, particularly when the rash is well pronounced, is that the intensity of the eruption is out of all proportion to the amount of constitutional disturbance. There is not present the prostration and high fever which would accompany a rash of similar severity in scarlet fever. Furthermore, there is never seen in scarlatiniform erythema a severe sore throat.

Another point of great diagnostic importance is the history as to previous attacks; the tendency to recurrence is a well-recognized feature of scarlatiniform erythema.

We have occasionally had patients sent into the Municipal Hospital with scarlatiniform erythemata which had been diagnosed as scarlet fever. We recall a young man who presented a generalized scarlatinoid eruption of moderate intensity which inaugurated the onset of a typical intermittent fever. Another patient, a girl aged five years, sent in from a foster home, had an eruption indistinguishable from scarlet fever, which proved to be a prodromal chickenpox eruption; this girl contracted a well-pronounced scarlet fever six days after admission to the scarlet-fever ward.

A young woman, sent into the hospital with an intense erythema which was diagnosed as scarlet fever, passed through an attack of exfoliative dermatitis, with profuse desquamation and subsequent loss

of hair and nails. She had previously received large doses of antipyrin, and this drug was found in the urine.

We have recently had under observation a young man, aged eighteen years, who was sent into the Municipal Hospital *three times within a year* with the diagnosis of scarlet fever. He was admitted to the Hospital first on June 3, 1902. He had vomiting, sore throat, slight fever, and a generalized scarlatiniform eruption. He desquamated profusely. The scaling lasted almost nine weeks, and the patient was discharged on September 3, 1902.

The patient was *readmitted* on January 9, 1903. He had sore throat, headache, slight fever, and a well-marked scarlatiniform rash. Slight desquamation occurred upon the face and trunk.

The patient was admitted for the third time on June 28, 1903. He had had repeated vomiting, headache, sore throat, and some fever; on admission there was a generalized, well pronounced scarlatiniform eruption, not punctated, however. The tongue was heavily coated, but after this disappeared there was no enlargement of the papillæ. Desquamation was well marked, being particularly copious on the hands and feet. The latter were still peeling in large lamellæ at the end of a month.

Each of these attacks resembled scarlet fever sufficiently to cause the resident physician to admit the patient.

We would call attention, however, to the fact that the fever and sore throat on each occasion were very slight. There was no prostration and the characteristic tongue was absent. We have no doubt that the patient was suffering from a scarlatiniform erythema, possibly due to intestinal autointoxication.

Drug Rashes.—Quinine, antipyrin, opium, belladonna, chloral, and mercury at times produce eruptions which may closely simulate that of scarlet fever. The eruption resulting from quinine is the most frequent and the most likely to be confounded with scarlet fever. As a rule, in these eruptions the constitutional disturbance is disproportionately slight, and severe sore throat, swelling of the glands, strawberry tongue, and middle-ear disease are absent. The eruption often fails to begin on the chest and pursue the normal progression of the scarlatinal exanthem. The occurrence of desquamation has no diagnostic value in these cases, as the drug rashes may be followed by a variable amount of epidermal exfoliation.

Measles.—There is no difficulty in distinguishing between measles and scarlet fever under ordinary circumstances. There are, however, irregular cases of each disease in which the elimination of the other in the diagnosis is by no means easy.

The rash in scarlet fever is now and then blotchy, especially upon the extremities; in other cases, particularly of septic scarlatina, a profuse rhinorrhœa may be present, even early in the course of the disease; these symptoms, associated with an otherwise irregular symptom-complex, may produce quite a resemblance to measles.

The eruption of measles may, as a result of coalescence of the macules,

closely simulate that of scarlet fever. In some epidemics the proportion of confluent measles eruptions appears to be greater than in others. A few years ago during the prevalence of a particularly severe form of measles, we noted a frequent tendency of the exanthem, after the lapse of twenty-four or forty-eight hours, to become confluent and present the appearance of a diffuse scarlatiniform eruption. Usually, however, there may be seen somewhere on the trunk or extremities sharp margination of the eruption with contiguous areas of pale, normal skin.

In measles the face is earlier and more copiously affected than in scarlet fever; the eruption is dusky red in color, palpably raised above the skin, and distinctly blotchy; it appears later than the eruption of scarlet fever (about the fourth day); there is a prodromal stage, during which time catarrhal symptoms affecting the eyes, nose, larynx, and bronchial tubes are present, producing watery eyes, sneezing, running nose, hoarseness, and frequent cough. The initial fever is not as high as in scarlatina and the tendency to vomiting is less. Sore throat, great glandular intumescence, strawberry tongue, lamellar desquamation, and nephritis, commonly seen in scarlet fever, are absent in measles.

The presence of Koplik spots upon the buccal mucous membrane would decide in favor of measles. The discovery of a marked leukocytosis would, it is claimed, point strongly toward the scarlatiniform nature of the disease.

At times a secondary roseolous or measles-like eruption appears later in the course of scarlet fever. This is regarded by Thomas as a pseudo-relapse, but it seems to us to be of the nature of a septic rash.

Smallpox.—Scarlet fever may be confounded with the prodromal scarlatiniform rash that is occasionally seen during the initial stage of smallpox. The absence of angina and the appearance of the variolous papules will make the diagnosis clear.

During the later pustular stage of variola an intense scarlatiniform eruption at times develops which may raise the question of a secondary infection with scarlet fever. There may be high fever, prostration, and subsequent desquamation. The absence of vomiting, sore throat, the strawberry tongue, and the development of the eruption about the twelfth to the fifteenth day of smallpox will usually enable one to recognize the character of the rash.

Influenza.—Influenza is sometimes accompanied by a scarlatiniform eruption which may cause scarlet fever to be suspected. The presence of severe muscular pains and catarrhal symptoms, and the absence of the angina and the characteristic tongue, together with attention to the character of the prevailing epidemic will usually suffice to distinguish the two affections.

Rubella.—With the usual type of rubella scarlet fever scarcely comes into differential conflict. It is with that form which tends to present a diffuse eruption that errors may arise. (See article on Rubella.)

Diphtheria.—Ordinarily scarlet fever and diphtheria have but little in common, and yet errors in diagnosis are not infrequent. Too often physicians glance into the throat, see exudate present upon the tonsils,

and perhaps upon the soft palate, and straightway make the diagnosis of diphtheria. Time and time again have we received calls at the Municipal Hospital for cases of diphtheria, only to discover on seeing the patient the presence of a scarlatinal rash. Diphtheria is ordinarily not accompanied by an exanthem.

Vomiting is much more common as an invasive symptom of scarlet fever than of diphtheria. The exudate in diphtheria is tough and thick, of a grayish or grayish-yellow color, and quite firmly adherent to the underlying mucous membrane. That of scarlet fever is yellowish, thin and smeary, and more easily wiped off. In scarlet fever, moreover, the throat ordinarily shows more intense redness and œdema than in diphtheria. The soft palate commonly presents a punctated, reddened appearance.

Enlargement of the maxillary and submaxillary glands occurs in both diseases. The temperature in diphtheria tends to subside in a few days; in scarlet fever it commonly persists for a longer period. The strawberry tongue of scarlatina is absent in diphtheria.

Otitis media may occur in both diseases, but it is more common in scarlet fever. Albuminuria is an *early* symptom in diphtheria and a *late* symptom in scarlet fever. It is present in about one-half or more of the cases of diphtheria and is commonly found on the third or fourth day. A transient albuminuria may occur early in severe cases of scarlatina accompanied by high fever, but the true scarlatinal nephritis is ordinarily discovered about the end of the third week. The early albuminuria of diphtheria is apt to be associated with the presence of tube casts.

While the finding of Klebs-Loeffler bacilli in the throat is of great diagnostic importance, their presence does not exclude scarlet fever. At the Municipal Hospital we have cultures made of all scarlet-fever patients on admission to the hospital. The percentage of cases in which diphtheria bacilli have been found varies from time to time. It has been as low as 8 in 100 and as high as 30 in 100. It is by no means always the bad throats that give positive cultures. In many of the cases in which the Klebs-Loeffler bacilli are found there is no exudate at all in the throat.

That diphtheria and scarlet fever may occur at the same time is generally admitted. In our experience scarlet fever has more often developed in the course of diphtheria than the reverse. Diphtheria is more apt to appear after the acute symptoms of scarlatina have subsided. Scarlet fever, on the other hand, not infrequently makes its appearance early in the course of diphtheria.

To distinguish between the scarlatiniform rash that occasionally occurs in diphtheria and a true complicating scarlet fever is a most difficult and, indeed, an often impossible task. Clinicians of experience recognize this fact. Osler, for example, says: "Scarlet fever and diphtheria may coexist, but in a case presenting widespread erythema and extensive membranous angina, with Loeffler's bacillus, it would puzzle Hippocrates to say whether the two diseases coexisted, or whether it was only an intense scarlatinal rash in diphtheria."

It has been our custom to regard as a complicating scarlet fever any well-pronounced scarlatiniform rash accompanied by distinct elevation of temperature; if vomiting occur and the lingual papillæ become enlarged the diagnosis is much clearer. We have sent all such cases to a mixed ward in which there have been undoubted cases of scarlet fever, and it has been extremely rare for any children thus transferred to contract scarlet fever. We have never seen an intense, well-pronounced scarlatiniform rash in diphtheria that we felt could be regarded as an erythema diphtheriticum.

Since the introduction of the use of diphtheria antitoxin the difficulties of diagnosis have been increased, for a third possibility presents itself, namely, a scarlatiniform antitoxin rash.

The occurrence of scarlatiniform eruptions in diphtheria wards is always a source of anxiety. If the patient is allowed to remain, other children may be exposed to scarlet fever; if, on the other hand, the patient is transferred to a mixed ward, there is a risk of his contracting scarlet fever. It is well to have nearby a number of small rooms in which patients may be placed for a few days and watched. These cases tax the diagnostic acumen of even the most experienced physicians.

Tonsillitis.—An inflammation and enlargement of the tonsils with the development of exudate in the crypts is so often seen in scarlet fever as to constitute a part of the symptom-complex of this disease. It is recognized that scarlatina may occur without an exanthem. The determination of the scarlatinal character of a tonsillitis occurring in a person exposed to the infection of scarlet fever is a most difficult matter. If the exposure has been intimate, the individual unprotected by previous attack of scarlet fever, the characteristic tongue appearance and the angina present, and otitis media or nephritis develop, the existence of angina scarlatinosa would be highly probable. Follicular tonsillitis not infrequently develops in persons exposed to scarlatina who have previously had the disease. Thomas says that all such cases should be regarded with suspicion, but we would hesitate to regard them all as scarlet fever. The symptoms are identical with follicular tonsillitis occurring from other sources. We have known persons unprotected by a previous attack of scarlet fever to contract, on exposure to the disease, what appeared to be an ordinary follicular tonsillitis; although no eruption was discovered in these patients, they have at times desquamated on the feet in a quite characteristic manner. Patients with sore throats of this nature have also been known to communicate scarlet fever to others. It is often impossible to determine with positiveness whether or not cases of follicular tonsillitis resulting from exposure to scarlet fever are to be regarded as angina scarlatinosa.

Occasionally an erythema develops in the course of an ordinary follicular tonsillitis. This eruption is often partial and may appear first on any part of the body. The exclusion of the diagnosis of scarlatina is only possible after a careful study of all of the symptoms, general and local, and attention to the circumstances of exposure and epidemic influence.

THE PROGNOSIS OF SCARLET FEVER.

The most important factor bearing upon the prognosis of scarlatina is the character of the prevailing epidemic. Some outbreaks of scarlet fever are of extreme mildness and others are frightfully severe. Sydenham never saw a severe case of the disease and, therefore, spoke of it "with a sort of contempt which he was far from having for measles or smallpox." According to Trousseau, his illustrious master, Bretonneau, had not seen a fatal case of scarlet fever from 1799 to 1822; he was, therefore, satisfied that "scarlet fever was the mildest of all the exanthemata." Later experience with a severe form of the disease caused him to change his opinion and regard the malady as equally mortal with plague, typhus, and cholera.

The character of scarlet-fever epidemics, as regards benignancy or severity, commonly persists for a period of years before a change in type occurs. Graves¹ has pointed out that a very fatal epidemic ravaged Ireland in 1800 to 1804. Then the type changed, and from 1804 to 1831 the affection was so wonderfully mild that scarcely any deaths occurred. In 1831, however, a malignant epidemic broke out and in a few years spread throughout Ireland, causing tremendous loss of life.

It is evident, therefore, that the mortality from scarlatina has an extremely wide range. It may fall as low as 3 per cent., or reach the frightful figure of 40 per cent. Johannsen states that in an epidemic in certain localities in Norway the death rate actually reached 90 per cent.; this murderous outbreak is absolutely without precedent.

Hirsch and Thomas hold that the average mortality of scarlet fever is about 10 *per cent.*; the more that the death rate exceeds this figure, the greater is the severity of the epidemic. When the death rate remains below 10 per cent., the epidemic may be looked upon as mild. Thomas, in enumerating the most fatal epidemics of scarlet fever, says Hambursin in Namur lost about 30 per cent.; Arrigoni about 40 per cent.; Salzmann, in Esslinger, from 1853 to 1857, about 36 per cent.; at Hornbach, in the Palatinate, in 1868 to 1869, 34 per cent.

The severity of scarlet fever has been diminishing within recent years. Johannsen says that among 84,580 reported cases in Norway there were 12,789 deaths, a mortality of 14.17 per cent. He regards the normal mortality in Norway as 13 per cent.

Caiger² states that during the past twenty-three years 81,350 cases of scarlet fever have been treated in the hospitals of the Metropolitan Asylums Board of London, with a combined mortality of 8 per cent. Since 1874 the annual percentage has progressively fallen from 12.2 to 5.9.

¹ Quoted by Trousseau, American edition, p. 137.

² Loc. cit., p. 128.

SCARLET-FEVER MORTALITY IN LONDON HOSPITALS. (CAIGER.)

Year.	Notifications.	Deaths.	General Mortality.	Hospital Mortality
1890	15,330	875	5.71	7.86
1891	11,398	589	5.17	6.67
1892	27,095	1174	4.33	7.25
1893	26,901	1596	4.32	6.11
1894	18,440	962	5.21	5.92

The higher mortality in the hospitals is said to be due to the larger proportion of severe cases sent in.

The death rate in the Municipal Hospital has been as follows:

SCARLET-FEVER MORTALITY IN THE MUNICIPAL HOSPITAL OF PHILADELPHIA.

Year.	Cases.	Deaths.	Percentage.	Year.	Cases.	Deaths.	Percentage.
1891	68	2	3.17	1898	380	45	11.84
1892	159	14	8.80	1899	604	57	9.43
1893	170	32	18.80	1900	645	58	9.20
1894	129	11	8.52	1901	1115	108	9.68
1895	168	11	6.73	1902	673	56	8.32
1896	258	18	7.11				
1897	358	99	10.37	Total	5213	506	9.72

It is seen from these figures that the mortality rate is somewhat higher in Philadelphia than in London.

The factors that influence the prognosis in individual cases are (1) the age of the patient, (2) the virulency of the infection, and (3) the character and severity of the complications.

Age.—Age affects the prognosis in a most striking manner. While the general mortality of scarlet fever is from 10 to 12 per cent., in children under five years of age, according to Holt, it is between 20 and 30 per cent.

In our own cases the general mortality among 5213 cases was 9.72 per cent.; in children under five years of age it was about double this figure—18.6 per cent.

The mortality for the different age periods of patients treated in the Municipal Hospital is herewith subjoined:

	Cases.	Deaths.	Percentage.
Under one year of age	40	13	32.5
One to five years	1670	305	18.22
Five to ten years	1766	106	6.0
Ten to fifteen years	476	19	3.99
Fifteen to twenty-five	295	18	6.10
Twenty-five and upward	133	7	5.27

The above table shows the highest mortality under five years of age, and particularly under one year. In the first year of life about one-third of our patients died.

After the age of five has been passed the mortality diminishes progressively. The death rate, in our own experience, reaches its minimum in children between the ages of ten and fifteen years.

Virulency of Infection.—Virulency of infection is indicated by great severity of the invasive symptoms. The prognosis is bad when the temperature is excessively high—106° or 107° F.; when convulsions, stupor,

or coma develop; when the eruption is irregular or partial in distribution, or when it is livid, suppressed, or hemorrhagic. These are malignant cases and the patient is, as a rule, overwhelmed early in the course of the disease.

During the first or second week the appearance of severe *anginose* or *septic* symptoms renders the diagnosis unfavorable.

Patients with a sloughy throat with tendency to gangrene, great lymphatic enlargement, purulent rhinitis, and otitis are apt to succumb to the poison of the disease.

Influence of Complications.—The complications which are most apt to cause death are nephritis, purulent otitis, meningitis, endocarditis, pneumonia, etc. The symptoms of evil omen in nephritis have already been referred to. It should be remembered that cases of scarlatina that begin in the most benign manner may develop a severe nephritis with its attendant dangers. This complication comes on late, during the third week, at a period when the patient and his family have perhaps looked forward to complete convalescence.

A favorable course of the scarlet fever may be anticipated, under ordinary circumstances, when the invasive symptoms are but moderately developed, when the throat is but mildly involved, when the eruption appears at the proper time, gradually reaches its maximum, and is uniformly distributed; when the fever steadily declines with the fading of the exanthem, and when complications are absent or of short duration.

In forecasting the result of an attack of scarlet fever, it is wise for the physician not to give an unqualifiedly favorable prognosis, even in mild cases; the liability to serious complications in this disease should cause him to make some reservation in the expression of an opinion as to the outcome of the illness.

THE TREATMENT OF SCARLET FEVER.

In the discussion of the treatment of scarlet fever, we shall take up first the *prophylactic* or preventive measures, then the hygienic care of the patient, and, finally, the direct treatment of the disease and its various complications.

Prophylaxis.—Scarlet fever is an endemic disease in nearly all great centres of population, and the health authorities of these commonwealths require sanitary regulations for the control and prevention of the disease.

As a prerequisite to the prosecution of this work compulsory *notification* is essential. The health authorities must know when and where scarlet fever exists in order to be able to check its farther extension. It is the custom in some cities to placard domiciles in which scarlet fever exists in order to warn persons who might be otherwise disposed to enter the infected houses. While this plan has certain distinct advantages it does not seem to have found favor among the general body of physicians. Boards of Health should have the power of thus labeling infected dwellings, but should exercise a discriminating judgment in

the employment thereof. When scarlet fever breaks out in a dwelling which is also used as a store or which communicates with one, the threatened use of the placard will often determine the tenants to send the patient to an infectious disease hospital.

In the event of refusal, the public should be apprised by means of the placard of the existence in the building of the disease in question.

There can be no doubt that many *infectious diseases are spread* through the mingling of children in *kindergartens and schools*. Scarlet fever almost invariably decreases during the summer vacation when the schools are closed, and increases again when the sessions begin. Every effort should therefore be made by the proper authorities to prevent the infection from being transmitted in the schools.

The procedure in vogue in most large cities at the present time is as follows: The head of the school is notified by the health authorities that one of the pupils is sick with scarlet fever, and that he is not to be permitted to return, save after certified examination by a medical inspector or some other duly authorized person. Other members of the same household that are in attendance at school should likewise be debarred until the patient has been sent to a hospital and the premises thoroughly disinfected, or until the patient has completely recovered from his illness and proper domiciliary disinfection has been carried out.

A child who develops an attack of scarlet fever should be debarred from school for a period of time *not less than two months*. Where nasal or aural discharge or desquamation persists beyond this period the enforced vacation must be still further extended. While such a rule often works hardship it will be found to best conserve the public health and welfare.

In large cities it is an excellent plan to have medical inspectors make frequent examinations of the pupils in the public schools, with a view to determining the existence of suspicious sore throats, late desquamation, etc. Where such medical service cannot be commanded, teachers should be instructed in the symptoms of scarlet fever, so that cases presenting suspicious symptoms might be immediately sent home. A careful and intelligent teacher may in this manner often discover the disease in its incipency and send the patient away before infection is conveyed to others.

If these precautions be carried out it will not be found necessary except, perhaps, in extensive epidemics to close public schools. The proper ventilation and cleansing of schools, rooms, and buildings will greatly lessen the danger of the transmission of contagious diseases.

Isolation.—The methods of isolation which are employed in checking the spread of infectious diseases in general can be utilized with much effectiveness in the prevention of scarlet fever. This is true (1) because but a very brief period elapses before the appearance of the characteristic eruption, thus making possible an early diagnosis, and (2) because the infection is not apt to be transmitted during the first few days of the disease. An opportunity is thus given to separate the patient from other members of the family, who may in this manner be protected. In this

respect scarlet fever differs essentially from measles, the contagium of which is given off at a very early date; it is much more difficult to protect persons who have been exposed to a case of measles than those who have been in contact with scarlatina during the early days. The contagious principle of scarlatina is much less diffusible than that of measles. This makes it possible to localize the infection more readily in a portion of a house or a hospital.

In households in which an effective isolation can be carried out, the protection of other members of the family can be accomplished with reasonable assurance. It must be recognized, however, under these circumstances that eternal vigilance is the price of safety. It is a safer plan to remove the well children to another place. The liability of their contracting the disease from an early and brief exposure and then carrying the infection with them is not very great. If there is fear that this will take place they can be detained at home, carefully separated from the patient for a week, which period will fully cover the stage of incubation.

Where effective isolation cannot be carried out at home, and this is the case in the large majority of households in a community, the patient should be sent to a *hospital*, the whole or part of which is set apart for the treatment of this disease. There can be no doubt that the treatment of scarlet fever in special hospitals is one of the most important means of preventing the spread of the disease. It is possible, with hospital-treated patients, to continue the isolation until every vestige of desquamation has disappeared, and until discharges from the nose and ears have ceased. This may in some cases require detention in the hospital for a period of twelve weeks or longer. In patients treated at home, especially among the poor, who are not so apt to recognize the responsibility of their actions, isolation for this period of time can seldom be enforced.

A very large number of cases of scarlet fever are doubtless contracted from patients who are prematurely permitted to associate with others. This naturally brings up the important question: *How long are scarlatina patients to be isolated and quarantined?*

This query is by no means easy of solution. Indeed, in no disease is it so difficult to affirm that the danger of infection has passed. The rule which is commonly followed is to continue the isolation until desquamation has completely ceased and the patient is free from nasal and aural discharges. In the average case this will cover a period of six or seven weeks. In some cases it will be necessary to extend the isolation beyond this period to eight, ten, twelve, or even fourteen weeks. Despite the utmost precaution in this respect, second cases will at times be infected at a late date.

All large scarlet-fever hospitals receive what are known as *return* cases. A certain small proportion, about 2 per cent. of the discharged patients, will give rise to cases of scarlet fever in the same household. The infection may be conveyed by patients who have been in the hospital nine, ten, eleven weeks or longer; this occurs even though

desquamation is complete, and the patient antiseptically bathed and clad in perfectly clean garments. The infection in these late cases is probably derived from the secretions of the nose, throat, or ears. We have already made mention of a fatal attack of scarlet fever contracted by a mother from a child who was discharged from the Municipal Hospital after a sojourn of nine weeks. This woman had been exposed to her child at an early stage of the disease, at which time she escaped infection. We have observed on a number of occasions that children who are exposed to the infection at an early period of the disease may escape only to contract the disease from a patient who is supposed to be free of contagion.

The Contagiousness of Desquamating Epithelium.—The view has generally been maintained that the infection in scarlet fever persists as long as there is any desquamation. Within recent years the contagiousness of the scales has been seriously questioned.

Millard,¹ in a thoughtful article, challenges the view that scarlatinal desquamation is infectious. The author obtained the opinions of a considerable number of experts whose answers he has formulated as follows: Sixteen gentlemen out of twenty-one state that (1) they can adduce no evidence that desquamating epithelium is, *per se*, a source of infection; (2) they consider that too much importance has been in the past attached to desquamation as a source of infection; (3) their experience does not support the popular view that desquamation after scarlet fever is necessarily an indication that a patient is still infectious; (4) they believe that a patient may continue to desquamate for some time after he has ceased to be infectious; and (5) they do not believe that it is necessary, in order to prevent the spread of infection, that patients who otherwise are quite ready to leave the hospital should be detained until every visible trace of desquamating epithelium has disappeared.

In conclusion the writer briefly sums up the principal arguments against the supposition that desquamation is infectious as follows: "1. The absence of evidence supporting it. It is difficult to believe but that if the old supposition were correct, strong evidence of it would ere this have been forthcoming, as is now the case with discharges from the nose and ears. 2. The fact that infectivity begins prior to the onset of desquamation and frequently continues long after desquamation has ceased. 3. The fact that scarlet-fever wards, although abounding in desquamation epithelium, are not a danger to neighboring houses. 4. The fact that the proportion of 'return cases' does not appear to be increased among patients sent out from hospital still desquamating. On the other hand, the principal argument in favor of the view that desquamation is infectious is the fact that patients still desquamating, but otherwise apparently free from infection, have frequently been known to convey the disease to others. The whole force of this argument disappears, however, when we consider that patients apparently

¹ The Supposed Infectivity of the Desquamation in Scarlet Fever, *Lancet*, April 5, 1902.

quite free from infection and in whom desquamation has entirely ceased have also been known to convey the disease; moreover, patients still desquamating have frequently mixed freely with others without untoward result."

There is much force in the arguments presented above. It is quite possible that during the process of desquamation the infection is not in the scales, but in the pharyngeal, nasal, and aural secretions. Not until the micro-organismal cause of scarlet fever is discovered will it be possible to satisfactorily solve this question. In the mean time if we err it should be upon the safe side, particularly as infection appears to reside in scarlatinal convalescents at a time that they are desquamating, and often for a long period subsequently.

As regards *second desquamation*, most observers do not regard it as capable of transmitting infection.

There are some apparent cases of transmission of the disease during second and third desquamation, but there is no proof that the scales conveyed the infection. The following cases were mentioned in a committee report of the Clinical Society of London:¹

Case 24.² On April 1, 1878, Master P. left school at Wimbledon, on the fortieth day of an attack of scarlatina, for his home at Brighton. Before leaving, desquamation had to all appearances quite terminated, the feet having desquamated twice. Also, he had repeated carbolic acid baths, and he had left all his infected clothes behind. After reaching Brighton his face and feet desquamated again and four days after his arrival his mother fell ill with scarlet fever.

Case 58.³ B., a girl aged nineteen years, slept one night with a cousin who was undergoing a second desquamation on the feet, eight weeks after the original attack. B. developed the scarlet-fever rash four days subsequently.

Hygiene of the Sick-apartments.—When a child is stricken with scarlet fever it should be immediately isolated. If it is to be retained at home a room or suite of rooms in the uppermost portion of the house is to be selected as the sick-apartments. Facilities for ventilation should be considered whenever a choice is possible. A room with an open fireplace is to be preferred, although such a convenience is seldom available. An excellent plan is to secure the ingress of fresh air through an adjoining room, the windows of which may be kept open for varying periods according to the season. This room should constitute the avenue of communication with other portions of the house.

Carpets, draperies, ornaments, and all dispensable articles of furniture should be removed from the room before occupancy by the patient. The spaces about doors communicating with other portions of the house should be sealed by pasting over them long strips of wrapping paper. Over the door communicating with the corridor should be suspended a sheet which is kept moistened with Labarraque's fluid, a 5 per cent. carbolic acid solution, or 1:1000 solution of bichloride

¹ Quoted by Millard.

² Communicated by Dr. Murchison in 1878.

³ Communicated by Dr. Whitelegge.

of mercury. Infectious particles floating in the atmosphere will adhere to the moistened sheet.

Great care should be exercised to keep the woodwork, furniture, and floors scrupulously clean; this is best accomplished by mopping with cloths saturated with one of the above-mentioned antiseptic solutions.

No one save the person selected to look after the patient should be permitted in the sick-room. If the mother acts as nurse she should devote her time exclusively to the patient and should not come in contact with any other members of the family. The nurse should not leave the sick-apartments except after complete change of clothing, bath, and shampooing of the hair with an antiseptic solution. Such garments should be worn by the nurse or mother as can be readily boiled or otherwise disinfected. The hair should be protected by a cap in order that it harbor as little infection as possible.

Recognizing that the scarlet-fever contagium is readily carried in clothing and upon various articles, it becomes the duty of the physician to take such precautions as to reduce the liability of transmitting the disease to a minimum. He should, before entering the sick-room, don a gown which extends from the neck to the feet. A cap should be worn to cover the hair, and it is a good plan, during the desquamative stage, to protect the shoes with rubbers. Upon leaving the patient the physician should wash the hands, face, beard, and exposed portions of the hair with an antiseptic soap.

Before visiting other children he should endeavor to get a thorough airing out-doors. It is best for physicians who happen to have obstetrical and scarlet-fever patients at the same time to relinquish the care of the one or the other.

That the above precautions are not superfluous is evidenced by the not infrequent carrying of scarlatina by physicians. Murchison investigated this subject and was informed by many physicians that they had conveyed the disease through their infected clothing.

Adult members of a household in which scarlet fever exists should safeguard the interests of others by avoiding contact with the world. The best guide under these conditions is the golden rule.

All articles coming in contact with the patient should be subjected to disinfection. In the room adjoining the sick-apartment should be kept a 5 per cent. solution of carbolic acid which should be used to cleanse utensils, body and bed linen, etc. The linen should be steeped in the antiseptic solution for an hour or two, then wrung out, placed in a receptacle outside the room, and finally cleansed with scalding water and laundered.

It is preferable when possible to retain the dishes and eating utensils within the sick-apartments. When they must be sent to other parts of the house to be cleansed they should first be immersed for half an hour in boiling water.

Discharges from the ears, nose, and throat should be received upon pieces of muslin or cheese-cloth, which should be burned or disinfected.

Where a sputum cup is used it should contain a solution of carbolic acid or chloride of lime; the same is true of urinals and bed-pans.

Disinfection.—After the termination of the illness the patient should be given an antiseptic bath of 1:10,000 bichloride of mercury. The head should be thoroughly washed with antiseptic soap and clean or new clothing put on. It is a wise precaution to prevent association of the patient with other children for several weeks after the quarantine has been raised. The disinfection of the sick apartments should be carried out with thoroughness. If perfunctory fumigation is relied upon to destroy all infection, unfortunate consequences may follow. The infection of scarlet fever has a remarkable tenacity and may remain resident in articles for months or years. Numerous instances of this are referred to in the chapter on Etiology.

All articles of little or no value in the sick-room should be burned. This is particularly true of those things with which the patient has been in contact, such as body-linen, books and toys.

The apartments should be thoroughly fumigated or sprayed, preferably with formaldehyde solution; as a matter of extra precaution this should be used in greater amounts than that ordinarily prescribed for the given air space. (See chapter on Disinfection.)

The floors, woodwork, and furniture should be vigorously scrubbed with a carbolic acid solution of about 1 part to 40. The walls, if painted, should be washed with the same solution. If the walls are covered with paper it is wisest to have them scraped and repapered.

Blankets, mattresses, upholstered furniture, clothing, etc., should be disinfected by superheated steam under pressure. Many large cities are now equipped with disinfecting plants to which all such articles may be sent. Where such is not the case the blankets and bed-linen after being fumigated had better be boiled and the mattress destroyed by burning.

It is a wise plan, whenever possible, to allow the sick-apartments to remain unoccupied and exposed for some days or weeks to the purifying influence of sunlight and fresh air.

The above precautions may be troublesome and expensive, but it is by careful attention to these matters that attacks of scarlet fever are often prevented and human life and faculties thus preserved.

In the event of death from scarlet fever the body should be enveloped in a sheet wet with a 1:1000 solution of bichloride of mercury. It should be placed in a hermetically sealed casket and buried at as early a date as possible. The interment should, of course, be private.

Care of Patient. Diet.—During the early days of scarlatina, when the fever is high, milk constitutes the best and usually the most acceptable diet. Cool milk is soothing to the throat and assuages the intense thirst which is present in severe cases. Most writers insist upon an exclusive milk diet throughout the entire febrile period, and many counsel its continuance during the early convalescent stage. When the patient is willing to take a sufficient quantity of milk to maintain his body weight there can be no objection to an exclusive milk diet; but

some children and many youths and adults object to the monotony of an exclusive milk diet. We have had an excellent opportunity of judging of the effect of diet in scarlet fever. For many years the scarlatina patients in the Municipal Hospital received an exclusive milk diet during the febrile period. For the past eight months, during which time over 500 patients were treated, the patients have had a more liberal dietary. They were encouraged to drink plenty of milk, but were permitted as soon as they cared to, to have bread and butter with their meals and a simple pudding and stewed fruit once a day. We found that patients desired nothing but the milk while the temperature was high, but that when it became lower they were eager to obtain bread and butter in addition. Our patients appeared to progress just as well under the enlarged dietary. Urinary examinations were made every other day and the results compared with those under the exclusive milk diet.

Albuminuria was not more frequent in the former than in the latter and the renal complications altogether were of a mild character. We present these facts for what they are worth. It is a hardship for some patients to be denied solid food for weeks, and they may as a result receive an insufficient amount of nourishment. We have never seen the above diet do any harm.

Caiger¹ allows patients, during the febrile stage, milk with eggs beaten up, broths, and calves-foot jelly. When the temperature falls he permits eggs, custard, light puddings, and bread and butter. Ripe and succulent fruit is given at any time throughout the illness. Caiger states that there is no risk, as has been alleged, of inducing a nephritis by permitting these articles of food to be taken.

Our present practice is to use an exclusive milk diet in infants and very young children and in cases of nephritis, but to allow older children and adults a little more latitude. The latter frequently request light solid foods, and we believe that when there is an appetite for such articles they do no harm.

Confinement to bed should be enforced during the febrile period, and, during cold and inclement weather, in severe cases for a week or more after the subsidence of the fever. Young and restless children whose actions cannot be well controlled had better be kept in bed from three to four weeks, or until the liability of nephritis has passed.

While it is generally believed that "catching cold" has been greatly exaggerated as a factor in nephritis, Griffith states that chilling of the surface certainly acts as a powerful accessory cause in the production of complications.

The detention of the patient in his bed or room will be influenced by the age of the individual, the season, and other factors which the discretion of the physician must solve.

In view of the liability to kidney complications, it is necessary to keep the skin, which is an important eliminatory organ, in a functionally

¹ *Loc cit.*, p. 170.

active state. All clinicians are agreed as to the advisability of employing sponge baths; tepid water is preferably used and should be applied twice daily. In addition to promoting gentle diaphoresis these baths subserve the ends of comfort and cleanliness.

To lessen the tension of the skin and allay itching the inunction of some unguentous substance is desirable. We have for years employed cacao-butter for this purpose and have found it cleanly and agreeable alike to nurses and patients. When much itching is present a 1 per cent. menthol or 2 per cent. carbolic ointment may be used.

Inunctions of salves containing oil of eucalyptus, ichthyol, certain silver salts, and many other substances have from time to time been lauded as possessing special therapeutic virtues.

Medical Treatment.—It must be frankly admitted that we possess no medicament capable of directly influencing or abridging the course of scarlet fever. Our therapeutic efforts must be directed toward combating excessive development of the symptoms and toward preventing and modifying complications. The treatment is, therefore, purely symptomatic in character.

In *mild* cases of scarlet fever special medication is often unnecessary, the disease progressing to a favorable termination under the influence of proper hygienic care and nursing.

During the febrile stage it is customary to administer a febrifuge mixture. We have been in the habit of using a combination of the liquor ammoniæ acetatis and sweet spirit of nitre, sweetened with a little syrup.

Vomiting, when present, may be controlled by abstinence from food and the administration of fractional doses of calomel. Constipation may be corrected by the latter drug, or one of the mild vegetable laxatives.

It is advisable to use some mild antiseptic in the throat, not only to relieve the congestion and soreness, but to lessen secondary infection and the liability of extension of inflammation to the middle ear.

Fever.—There are many cases in which attention must be directed to the control of high temperature and the accompanying nervous phenomena. Scarlet fever is frequently characterized by a very high initial pyrexia, which tends in a few days to defervesce. When the fever is above 103° F., and particularly when there are severe nervous symptoms, such as headache, delirium, stupor, or convulsions, antipyretic measures should be employed. In the reduction of temperature preponderant reliance is now placed upon *hydrotherapy*. Different clinicians have individual preferences as to the mode of applying water; the methods in vogue are tepid sponge baths, cold sponge baths, wet or cold packs, and warm, graduated, or cold tub baths. Ice-bags and Leiter's coils are also employed.

The routine treatment of scarlet fever with cold tub baths, as in the case of typhoid fever, has not met with general favor. They may be employed in cases accompanied by great hyperpyrexia, provided there is no pronounced cardiac depression. Cold baths are not borne well

by infants or very young children, and should not be used in such cases.

In cases of average severity with high fever, sponging with cold water, with or without alcohol, will usually suffice to keep the temperature within proper bounds. If this does not control the fever and nervous symptoms, resort may be had to the cold pack, which has a more pronounced antipyretic influence. In milder cases it may be all sufficient to keep an ice-bag or cold coils applied to the head.

Warm tub baths of about the temperature of 95° F. are recommended by many physicians. These will frequently reduce a high temperature, and are more acceptable to the patient and the members of his family than cold baths; or the graduated bath may be used, the temperature gradually being lowered until the desired reduction in the fever is accomplished.

The old superstition about baths being dangerous and causing patients to "catch cold" has been dissipated, and a complete unanimity of sentiment now exists among physicians as to the desirability of using baths of one kind or another in scarlet fever.

Medicinal antipyretics are used to a very limited extent nowadays. The general feeling is that they are dangerous in large doses and ineffective in small amounts. Phenacetin in small doses (2 to 3 grains) may be given as an adjunct to hydrotherapy in bad cases, or to relieve headache and nervous symptoms in milder cases. Antipyrin and acetanilid are not in favor, as they are apt to cause too much cardiac depression.

Throat.—Where the throat shows but slight involvement mild antiseptic fluids may be employed, either in the form of a spray or a gargle. For this purpose a weak Dobell solution or a solution of boric acid or chlorate of potash may be employed. Very young children cannot use a gargle, and often vigorously object to efforts at swabbing or spraying the throat. Where the physical resistance is so pronounced as to exhaust the child the procedure is of doubtful advantage and had better be discontinued. In the anginous variety of the disease it is equally important to cleanse the nares and throat and to avoid an exhausting resistance. A firm and skilful nurse is of great assistance under such circumstances.

When the throat is severely involved and a streptococcus pseudo-membrane is present, systematic and vigorous treatment is indicated. Not only does the pharyngeal inflammation tend to spread to the nares and middle ear, but a general infection is apt to result from streptococcal absorption.

In these cases the throat should be frequently sprayed with peroxide of hydrogen, plain or diluted, according to the age of the patient and the degree of inflammation present in the fauces.

In septic cases with ulceration of some of the soft tissues, Caiger¹ speaks in terms of high praise of a strongly acid solution of chlorate of

¹ Loc. cit., p. 171.

potash containing a large amount of free chlorine.¹ The throat and nose are irrigated with this fluid by means of a soft-rubber syringe with a vulcanite nozzle, the head being held over a basin with the mouth kept open.

Caiger says: "No amount of gargling, spraying, or swabbing can compare with it (this method) in point of efficacy."

Forchheimer speaks highly of direct applications to the throat by means of a swab saturated with Loeffler's iron-toluol solution. This should be applied once or twice a day and held in contact with the diseased parts for a little while to secure the best results. In cases of extensive streptococcic exudate in the throat this writer counsels the use of antistreptococcus serum, which, he believes, will occasionally improve the local symptoms in a remarkable manner.

Purulent Rhinitis.—Purulent rhinitis in scarlet fever is apt to accompany severe throat involvement. The extension of the suppurative inflammation to the nasal mucous membrane increases the liability to general sepsis and augments the gravity of the disease. A sanious, sero-purulent discharge issues from the nostrils in great quantities. The efforts of the nurse must be directed toward systematic and frequent cleansing of the nasal cavities. But this must be done with great care and gentleness. The forcible projection of liquids into the nose will do harm, as will, likewise, the use of strong and irritating antiseptics. It has been our custom to have the nose gently irrigated with a warm saline solution; this is done with a small glass piston-syringe with a blunt end. In obstinate cases we have recently employed a 10 per cent. solution of argyrol, one of the newer silver compounds. This remedy has lessened the profuse discharge and has led to a healthier condition of the parts.

Patients with gangrenous destruction of the soft palate or tonsils do not, as a rule, recover. Apart from the stronger remedies referred to in the treatment of membranous angina, one may, in this condition, employ a warm solution of permanganate of potash, 1:2000. In circumscribed gangrenous patches we have frequently applied the tincture of iodine with good results.

Noma.—Noma is fortunately an uncommon complication of scarlet fever. When the condition is still in its incipency the pultaceous deposit upon the mucous surface should be scraped away with a curette and the base thoroughly cauterized with fuming nitric acid. This had better be done under the use of ether, which can be given in just sufficient quantity to benumb the patient's sensibilities. If the cutaneous surface becomes attacked, free excision will be found to be a not too radical procedure.

Glands.—The glands at the angle of the jaw commonly attain the greatest size and most frequently undergo suppuration. Glandular

¹ According to Caiger the solution is prepared by pouring strong hydrochloric acid upon powdered chlorate of potash in a large, stoppered bottle. The proportions advised are 5 minims of strong acid to 9 grains of the salt, with sufficient water to make an ounce. The solution is of a greenish color, and has a strong chlorine odor.

abscess may be expected in nearly all cases of anginose scarlatina. In the beginning an ice-bag should be applied about the neck. A special bag manufactured for this purpose buttons around the neck and keeps the ice in close apposition with the affected glands. A piece of flannel should be interposed between the bag and the skin. A dried pig's bladder filled with small pieces of ice will answer the purpose when an ice-bag is not available.

If, despite the application of cold, the gland increases in size and suppuration becomes inevitable, heat should be substituted. Flaxseed poultices, rendered antiseptic by having incorporated in them a 1:4000 solution of corrosive sublimate, hasten the suppurative process. Upon the first suspicion of pus formation an incision into the gland should be made and free drainage established. It is better to lance prematurely than to delay too long, for inflammation may spread to the periglandular tissues. When cellular infiltration takes place free incisions should be made, even though no pus focus can be demonstrated, for by this means the deep-burrowing pus which forms later may be anticipated and the most fatal of complications—Ludwig's angina—may be prevented.

The Ears.—Inasmuch as otitis media is an extremely common complication of scarlet fever, it should be guarded against as much as possible and the condition promptly met when it develops. The prophylactic treatment relates to those measures which are designed to keep the nasopharynx clean and free of infective secretions. While this object is a laudable one, no treatment will, in bad cases, prevent the development of otitis media. Indeed, it may be stated that the liability to ear complications is directly proportionate to the severity of involvement of the throat and nose.

Pain in the ear is best relieved by the application of heat; this may be accomplished by syringing gently with water as hot as can be borne, or, better still, by the use of external dry heat. The hot-water bag or hot salt or bran bag may be placed against the ear. Dench suggests heating a little salt in the tip of a kid-glove finger and thrusting the same into the ear. The instillation of a few drops of a warm 4 per cent. solution of cocaine is advised by some writers.

When the pain continues despite these measures, suppuration is probable. If upon inspection of the tympanic membrane bulging is seen, an incision should be made to evacuate the pus. It should be remembered, however, that in very young children, in whom otitis is commonest, the small size of the canal and the restlessness of the patient make aural inspection and paracentesis extremely difficult and unsatisfactory. Furthermore, spontaneous rupture is the rule in these cases, and may be the first evidence of involvement of the ears.

After drainage is established it is necessary to keep the external auditory meatus clean and free of pus. Various liquids are advised, such as 1:5000 solution of bichloride of mercury, 1 in 4 solution of peroxide of hydrogen, saturated solution of boric acid, etc. We have found boiled water containing a little carbolic soap very useful. All solutions should be used warm and injected gently with a soft-rubber

bulb ear syringe. The meatus should not be plugged with cotton. Sudden rise of temperature indicates a stoppage of drainage or extension of inflammation to adjacent structures. Any swelling in the mastoid region should be promptly and freely incised and proper drainage maintained. There should be no hesitancy about entering the mastoid antrum if the bone exhibits evidence of disease. In all such cases the services of an aural surgeon should be called into requisition.

Joints.—Scarlatinal synovitis or arthritis (scarlatinal rheumatism) calls for both local and constitutional treatment. Physicians are not all in accord as to the value of the salicylates in inflamed joints in this disease, although many testify to their efficiency. Where the joint involvement is pronounced they should be given a trial; if no improvement is noted, or if the stomach is deranged or the heart depressed, their administration had better be interrupted. The inflamed joints should be painted with tincture of iodine, surrounded by cotton-wool and bandaged with a flannel bandage. Increase of fever, chills and sweats, with aggravation of the local symptoms, indicate the presence of pus in the joints. The joints should be incised, through and through drainage established, and the cavity washed out with antiseptic solutions. When there is doubt as to the presence of pus, the aspirating needle may be used and a small quantity of fluid drawn out. When streptococci are present in the synovial fluid the use of antistreptococcic serum is advised. During convalescence from articular complications care should be taken to preserve the mobility of the joint by gentle massage and passive movements. In all cases of joint involvement the heart should be carefully watched, for cardiac complications are much more common under these circumstances.

Kidneys.—Nephritis is one of the most common and most serious complications of scarlet fever. It not infrequently occurs in mild cases, at a time when the patient is considered almost well. It is a good plan to keep patients in bed for at least three weeks, as it is during the third week of the disease that nephritis is most frequently discovered. The urine should be examined each day for both albumin and tube casts. Ordinarily the chemical and microscopic examinations of the urine will enable one to determine the onset of a nephritis. In rare cases sudden and alarming symptoms may develop without the previous occurrence of albuminuria. It is of importance, where nephritis is suspected, to have the quantity of urine excreted in each twenty-four hours carefully measured. Pallor, puffing of the face, and elevation of temperature are among the early clinical evidences of oncoming nephritis.

When albumin is found the patient should be kept in bed and the temperature of the room kept warm and equable. The diet should be restricted to milk, which, with water, the patient should be encouraged to drink in large quantities. The bowels should be kept freely open and the action of the skin encouraged by daily warm baths. Under this simple regimen the vast majority of cases will make a good recovery.

If the urine is reduced in quantity and the symptoms do not improve,

a more active treatment should be pursued. We have found the use of a diuretic mixture containing infusion of digitalis and acetate of potash of especial value. Calomel may be given in sufficient dosage—about $\frac{1}{4}$ gr. three times a day—to produce two or three movements a day; this drug has the advantage of increasing renal secretion at the same time. It is an excellent plan to place over the kidneys a warm poultice composed of 1 part of ground mustard to 15 parts of flaxseed meal. This should be renewed every two or three hours.

Vomiting, flushed face, and a high-tension pulse indicate the use of nitroglycerin. This drug may be administered to children in the dosage of $\frac{1}{800}$ to $\frac{1}{200}$ gr. every few hours until the physiological effect is produced.

The development of uræmic symptoms such as twitchings, delirium, or stupor necessitates vigorous treatment. Free but not excessive catharsis should be produced by calomel or salines. The patient should be given a *hot pack* or a *hot vapor* or *hot-air bath*. In using the pack the patient is enveloped in a blanket which is wrung out of water of 100° F. temperature; this is surrounded by a dry blanket and this in turn by a rubber mackintosh. After free sweating is induced, the blankets can be removed and the patient rubbed dry. The *hot pack* may be used twice a day.

In the hot air bath the patient is enveloped in blankets between the folds of which are placed hot bricks or bottles. Where these measures do not suffice, pilocarpine may be given hypodermically. The dose varies from $\frac{1}{80}$ gr. to $\frac{1}{12}$ gr. according to age; for a child five years of age $\frac{1}{80}$ gr. may be given. Owing to the frequent depressing effect of this drug in children its administration had better be preceded or accompanied by alcoholic stimulation. It is advised that pilocarpine be withheld in cases in which there is profuse bronchial secretion, to avoid a possible pulmonary oedema.

If convulsions develop the hydrate of chloral should be given either by the mouth or bowel. A hypodermic injection of morphine is often of great value. If the convulsive seizures are persistent they should be controlled by inhalations of chloroform. In desperate cases it is well to perform venesection and follow the abstraction of blood by the intravenous injection of salt solution.

Alarming symptoms may result from oedema of the lungs or from effusion of serum into the pleural or pericardial sac. These conditions must be borne in mind and carefully watched for.

A certain degree of anæmia is apt to follow severe cases of nephritis. For this condition iron in the form of Basham's mixture will be found to serve a useful purpose.

After a severe nephritis great care should be exercised concerning the patient's diet and hygiene. The urine should be carefully examined at frequent intervals. If albuminuria persists and becomes subacute, the child should, if possible, be sent to a warm climate, where he should remain during the winter months. Every precaution should be taken to protect the patient against exposure.

The Heart.—In severe cases of scarlet fever it is frequently necessary to support a flagging heart. When the first sound is weak or the pulse is rapid, small, or irregular, cardiac stimulation is imperative. The majority of cases of scarlet fever will not require the use of alcohol, but one should not hesitate to use a good brandy or whiskey in full doses when the heart gives evidence of failing power. Digitalis will serve a useful purpose when the stomach is tolerant. When digitalis is not well borne, strophanthus may be substituted. Strychnine in $\frac{1}{200}$ to $\frac{1}{100}$ gr. doses will often be found valuable. When the peripheral circulation is feeble, resort may be had to hypodermics of nitroglycerin, gr. $\frac{1}{300}$ to $\frac{1}{200}$, every few hours. The subcutaneous injection of camphor dissolved in ether or almond oil may tide over a threatened collapse.

Endocarditis and pericarditis develop most commonly in association with scarlatinal rheumatism. Involvement of the joints should cause one to be vigilant concerning cardiac complications. Upon the first suspicion of valvular trouble an ice-bag should be placed over the heart and the salicylates should be cautiously administered or continued if they were previously being used. The patient should be kept at perfect rest in a horizontal position. We have seen sudden dilatation of the heart result from the patient sitting up. If pericarditis with effusion is present, it may become necessary to attempt an evacuation of the pericardial fluid.

Gastrointestinal Tract.—The early vomiting is seldom persistent; when treatment is necessary, abstinence from food, the swallowing of pellets of ice, and the administration of fractional doses of calomel will control the emesis. Early diarrhœa need not be interfered with if it is mild. If it is severe it may be controlled by the use of bismuth, vegetable astringents, and, if necessary, opium. The same treatment should be applied to profuse bowel movements developing late in the disease. If the inflammation is in the large intestines, irrigation of the colon with a warm saline solution or mild astringents and antiseptics will be found useful.

Purpura.—Hemorrhages into the skin and from the nose, mouth, kidneys, bowels, etc., may develop during the second or third week of scarlet fever. The patients become extremely anæmic and may die from the loss of blood. In a case under our care of purpura with epistaxis and bleeding from the mouth and kidneys, the patient gradually going from bad to worse, rapid improvement followed the administration of turpentine. Five minims of turpentine were given in an emulsion of acacia and elixir of orange, every two or three hours. The hemorrhage stopped in less than a day and the patient made a good recovery, the previously existing nephritis not being aggravated by the turpentine. This drug is highly recommended in purpura by Crocker, of London. Ferruginous preparations are indicated in the anæmia that follows these attacks.

Malignant cases of scarlet fever, characterized by a mottled and cyanotic surface, cold extremities, with or without high internal fever (as indicated by the rectal temperature), require vigorous stimulation.

A hot mustard bath should be given to increase the peripheral circulation and lessen internal congestion. Trousseau counselled the use of ammonia and musk in this condition. Jacobi advises the use of ammonia, musk, and camphor, and considers these drugs superior to alcohol. He also recommends in these cases, when the temperature is low, the use of morphine in doses of $\frac{1}{80}$ to $\frac{1}{40}$ of a grain, repeated according to effect.

In malignant attacks and also when uræmia is threatened it is advisable to employ *subcutaneous* or *intravenous injections* of a *decinormal saline solution* ($\frac{6}{100}$ per cent. solution of sodium chloride in sterilized water); 200 to 500 c.c. may be injected in a child. In uræmia the injection may be preceded by venesection.

Serotherapy.—On account of the great frequency with which streptococci are found in the throat and in various organs which are the seat of complications in scarlet fever, attempts have been made to make an *antistreptococcus serum* to combat the complications and even the disease itself.

Marmorek prepared an antistreptococcus serum which has been used to a considerable extent in this disease. The results are inconclusive and not particularly encouraging. Josias, in 1896, used the Marmorek serum at the Trousseau Hospital with disappointing results. The serum cases appeared to do no better than a control series of cases receiving no serum. Baginsky employed this same serum without benefit. Forchheimer used the serum as a routine practice in a limited number of cases of scarlet fever. The serum did not affect the course of the disease in any way, but occasionally the local symptoms of streptococcus angina were improved most remarkably.

More recently Moser¹ has employed a new antistreptococcus serum. He states that among 669 cases of scarlet fever in the St. Anna Hospital in Vienna, 81 received the serum. Among cases receiving injections on the first and second days of the disease there was no mortality. Later injections gave a gradually rising death rate: third day, 14.29 per cent.; fourth day, 23.88 per cent.; fifth day, 40 per cent. Moser states that the clinical symptoms improve promptly after the serum is introduced. The different pus processes and nephritis are lessened in frequency, but not altogether prevented. The mortality among 400 cases of scarlet fever in the St. Anna Kinderspital in 1901 was 8.9 per cent., as against an average mortality for scarlatina of 13.09 per cent. in other hospitals in Vienna in which serum was not used.

Baginsky has attacked Moser's conclusions as to the value of his serum. Baginsky has treated 50 cases of scarlet fever with a serum made by Aronson from a throat streptococcus, and from one obtained from bone-marrow from a scarlatinal subject. Of these 58 cases, 3 died, giving a mortality of 4.2 per cent. Including moribund cases and several cases that died from other causes, there were 62 cases with 7 deaths, or 11.3 per cent. mortality. As compared with this series there were 63 not treated by serum, of whom 9 died, a mortality of 17.3 per cent.

¹ Berliner klin. Wochenschrift, October 20, 1902, p. 996.

Baginsky is inclined to look favorably upon the serum treatment, although the results thus far have not been very striking.

USE OF BLOOD SERUM OF CONVALESCENTS.—Roger¹ reports the case of a boy, aged fifteen years, suffering from an extremely severe scarlet fever, who entered the hospital on the second day of the disease. A hypodermoclysis of 400 grams of saline solution was administered. The patient was semicomatose, pulse 120, respirations 68, and temperature 40.2° C. Urine almost suppressed. The prognosis was almost hopeless. A convalescent was bled and 100 grams of blood recovered. This was rapidly defibrinated and 80 c.c. injected beneath the skin of the patient's abdomen, after venesection had been performed upon him. Five hours later the patient was sleeping quietly and breathing more easily, but still in a dangerous condition, with suppression of urine. The patient was given a bath to reduce the temperature and saline solution was again injected. The following day the patient was completely transformed; consciousness returned; the patient spoke freely, felt well, and asked for food. The patient made a good recovery. Roger remarks that he never saw such a rapid recovery after so grave a case.

Hüber and Blumenthal² also used human blood serum in scarlet fever. They obtained the serum by venesection of convalescents from four to twenty-one days after the subsidence of fever. The blood was immediately mixed with an equal amount of a sterile saline solution and 1 per cent. of chloroform added. It was then vigorously shaken and allowed to stand for twenty-four hours. It was then strained through linen and filtered through a Berkefeld-Nordmeyer apparatus. Thirteen cases of scarlet fever were injected with this serum, 20 c.c. to 40 c.c. being employed. In only 3 cases was a positive beneficial result noted; in 8 cases the result was not very pronounced.

More evidence is needed before any conclusions can be drawn as to the value of this method of treatment.

Baginsky has used *Credé's ointment* of colloidal silver in the treatment of a number of grave cases of scarlet fever. The cases were septic ones of unusual severity, and but 3 out of the 13 recovered. The results were disappointing and serve to negative the claims made for this method of treatment.

¹ *Presse méd.*, 1896, iv. p. 245; also *Les maladies infect.*, p. 1372.

² *Berliner klinische Wochenschrift*, 1897, No. 31.

CHAPTER IX.

MEASLES.

Definition.—Measles is an acute, contagious, febrile disorder, characterized by catarrhal symptoms affecting the upper respiratory tract, and an eruption of dusky-red, slightly elevated macules. The disease commonly occurs in epidemics and attacks for the most part children; one attack confers immunity in the vast majority of cases.

Synonyms and Derivation.—*Rubeola, morbilli*; French, *la rougeole*; German, *masern, flecken*. Italian, *morbili, rosalia*; Spanish, *scrampion*.

The word measles is probably derived from an old English word, *maseles*. Hirsch calls attention to the resemblance to the German *masern* and the Sanskrit *masura*, meaning spots. The term *morbili* is derived from the Italian *morbillo*, which signifies the *little disease*. This diminutive was doubtless employed to distinguish measles from smallpox, the plague, *il morbo*, probably referring to the latter affection.

History.—It is impossible to state with any degree of positiveness the date of origin of measles. Some writers have attempted to prove that measles existed in the days of Hippocrates, but such an assertion does not appear to be warranted by the writings of the Greek and early Roman physicians. The references in the medical literature of this period are so vague as to offer a very inadequate basis for the belief that they refer to so clear-cut a disease as measles. Most writers concur in the opinion that both measles and smallpox definitely made their appearance about the tenth century. They appeared to have had their origin in the countries bordering on the Red Sea, and from this region to have spread westwardly throughout Europe. The first clear mention of measles is attributed to that master Arabian physician, Rhazes, who lived about A.D. 910. His distinguished successors, Ili Abbas and Avicenna, described measles under its Arabic designation, *Hasba*, or *al hasbet*. The term *rubeola* was later brought into use by the Latin translators of the Arabian writings. *Morbili* was very loosely applied to many exanthematous conditions.

The Arabian physicians regarded measles as a variety of smallpox. Willan¹ attempted to identify in the writings of Hippocrates and other early writers references to smallpox and measles, and quotes the description of Serapion, an Arabian physician.²

Avicenna looked upon measles as a bilious smallpox. Sennertus in 1640 proposed as a subject of enquiry the reason why the disease in some constitutions appeared as smallpox and in others as measles.

Diemerbroeck, in a posthumous work published in 1687, says: "The matter by which the measles is generated is not so thick as in the case

¹ Robert Willan's Miscellaneous Works, edited by Ashby Smith, London, 1821, p. 46.

² Theorice, lib. viii. cap. 14.

of smallpox. It is drier and somewhat choleric." He regarded measles and smallpox as different varieties of the same disease.

Sydenham, although a contemporary of the Dutch physician just quoted, was a much closer observer. He carefully studied the symptoms of measles during the epidemic of 1670-74, and his description of the disease (barring a few terms, for instance the use of the word pustule) compares not unfavorably with present-day writings: "The measles generally attack children. On the first day they have chills and shivers, and are hot and cold in turns. On the second day they have the fever in full—disquietude, thirst, want of appetite, a white (but not a dry) tongue, slight cough, heaviness of the head and eyes, and somnolence. The nose and eyes run continually, and this is the surest sign of measles. To this may be added sneezing, a swelling of the eyelids a little before the eruption, vomiting, and diarrhoea with green stools. These appear more especially during teething time. The symptoms increase until the fourth day. Then, or sometimes on the fifth, there appear on the face and forehead small red spots, very like the bites of fleas. These increase in number and cluster together, so as to mark the face with large red blotches. They are formed by small papulæ, so slightly elevated above the skin that their prominence can hardly be detected by the eye, but can just be felt by passing the fingers lightly along the skin.

"The spots take hold of the face first, from which they spread to the chest and belly, and afterward to the legs and ankles. On these parts may be seen broad, red maculæ, on but not above the level of the skin. In measles the eruption does not so thoroughly allay the other symptoms as in smallpox. There is, however, no vomiting after its appearance; nevertheless there is slight cough instead, which, with the fever and the difficulty of breathing, increases. There is also a running from the eyes, somnolence, and want of appetite. On the sixth day, or thereabouts, the forehead and face begin to grow rough as the pustules (?) die off and as the skin breaks. Over the rest of the body the blotches are both very broad and very red. About the eighth day they disappear from the face and scarcely show on the rest of the body. On the ninth there are none anywhere. On the face, however, and on the extremities—sometimes over the trunk—they peel off in thin, mealy, squamulæ, at which time the fever, the difficulty of breathing, and the cough are aggravated."

To Sydenham belongs the distinction of trenchantly separating smallpox and measles. But scarlatina and measles were still confounded. Twenty years later Morton regarded measles and scarlet fever as due to the same miasm; he asserted that they bore the same relation to each other as discrete and confluent smallpox. Many writers of this period spoke of scarlatina under the designation of *morbilli confluentes*.

Reports of epidemics which were undoubtedly measles were, according to Fuchs, published by Forestus (1563), Lange (1565), Ballonius (1574-75), and Schenk (1600).

As far as any accurate knowledge is concerned, measles is a disease of comparatively modern origin.

THE ETIOLOGY OF MEASLES.

Measles may be regarded as the most contagious of the various exanthematous affections. When it breaks out in a household or an institution it is almost impossible to prevent its spread, so diffusible is the contagious principle which causes it. This fact and the universal susceptibility to the disease make measles the commonest malady to which human flesh is heir. But few persons go through life without at some time or other passing through an attack of measles. When it is escaped during childhood it is extremely apt to be contracted during adult life; in this respect it differs markedly from scarlatina, against which most adults acquire an immunity.

Whether or not measles can be successfully inoculated still remains in doubt, despite the very considerable experimentation and literature on the subject.

In 1758, Francis Home, of Edinburgh, attempted the inoculation of measles at the suggestion of Monro. He saturated bits of muslin with blood obtained by incising through the measles lesions. These were laid open upon the excoriated arms of healthy persons. In this manner he claims to have inoculated twelve children, in most cases with success, although the disease appeared in a mild form. Pieces of muslin moistened with the nasal secretion which were placed in the nostrils of healthy children failed to produce the disease. Theussink,¹ who attended Home's clinics and saw these experiments, expresses doubt as to Home's interpretation of the results. At Theussink's suggestion, his friend Themmen later repeated these inoculations in 1816 with negative results.

In 1822 Speranza successfully inoculated measles, and claims to have had the disease himself in this manner. In 1854, an Italian physician, Bufalini, reported successful results both of his own and his countrymen, Locatelli, Rossi, and Figueri; Horst and Percival are likewise credited with positive inoculations.

In 1842 Katona² performed 1122 inoculations in twenty-six townships of the Borsoder Comitatus; 93 per cent. of these were successful, the attacks being of a mild character. An admixture of blood and the contents of miliary vesicles taken at the height of the rash was rubbed into excoriations made after the manner of vaccination. At the end of seven days fever and the usual prodromal symptoms developed; the eruption appeared two or three days later, about the ninth or tenth day after the inoculation.

Mayr successfully inoculated measles in 1848 and in 1852. He placed freshly secreted nasal mucus from a case of measles in the nostrils of two children living at a distance from one another. At the end of eight and nine days, respectively, catarrhal symptoms developed, followed in a few days by fever and the eruption. In an article on measles³ published

¹ Abhandlung über die Masern, translated from the Dutch by Dr. Doden, of Göttingen.

² Nachricht von einer im Grossen erfolgreich vorgenommenen Impfung der Masern während einer epidemischen Verbreitung derselben, Österreich. med. Wochenschrift, 1842, No. 29, pp. 697-98.

³ Mayr's article on Measles in *Hebra's Diseases of the Skin*, 1866.

in 1866, Mayr remarks: "Inoculations with blood made by myself in 1848 and 1852 afforded negative results." The use of desquamating skin also failed to transmit the disease, as had previously occurred in the experiments of Alexander Monro. The negative results in the transmission of measles by the inoculation of blood, in the hands of Themmen, Albers, Mayr, and Thomson, should cause us to accept the alleged successful results with some reservation. Only after there has been confirmation by perfectly reliable and careful observers, under conditions that preclude the possibility of the natural transmission of the disease, should measles be regarded as an inoculable affection.

The usual mode of contagion in measles is by *direct exposure* to a person suffering from the disease. The contagium of measles differs from that of scarlet fever in two respects—it is *more diffusible* and it is *less tenacious*; the infection does not tend to any marked degree to cling to objects or apartments, and transmission of the disease by fomites is, therefore, distinctly unusual.

Richard¹ claims that the contagium of measles cannot be carried by fomites nor by a protected person. Bard² states that the contagium of measles does not remain viable in a locality from which patients have removed. Comby³ says that the germ of measles has but little vitality outside of the body, and that every germ that emanates from a measles patient is dead at the end of a few hours.

While we are not prepared to dogmatically state that measles cannot be carried by infected objects or third persons, our experience is in accord with that of most writers that such occurrences must be very rare. Von Kerchensteiner calls attention to the observation that physicians' children do not as a class contract measles earlier in life than other children. Considering the frequent neglect of precautionary measures, this would not be the case if the disease were readily transmissible through infected garments.

Official reports of the extensive epidemic of measles in the Faroe Islands in 1846 (at which time over 6000 persons were attacked) gave no instances of transmission of the disease by infected articles or by third persons, and this point was carefully investigated by the physicians who studied this epidemic.

Theussink states that he knew of a case where the infection was conveyed by a letter sent through the post, and also an instance where it was attributed to an engraving sent by mail. The negative evidence of intermediate infection is so abundant that such cases must be substantiated beyond the peradventure of a doubt before they can be unreservedly accepted.

When measles breaks out in a family circle it attacks all of the susceptible members thereof. Kindergartens and schools offer fertile opportunity for the dissemination of diseases. Consequently measles, as well as the other contagious diseases of children, is much more

¹ Therapeutic Gazette, July 16, 1888.

² Revue d'hygiène et de Police Sanitaire, May 20, 1891.

³ Traité des mal. de l'enfance.

common during the periods of the year that these institutions are in session.

Susceptibility to measles is *practically universal*. All mankind, almost without exception, will take the disease when exposed to it. The temporary insusceptibility exhibited by very young infants will be referred to later.

One of the most remarkable and instructive epidemics of measles in history is that which visited the Faroe Islands in 1846.¹ These islands had been free from measles since 1781, a period of sixty-five years. The disease was introduced by a Danish cabinetmaker who had become infected in Copenhagen. On his arrival at Thorshavn, the chief port of the islands, he communicated the disease to two friends. These persons gave rise to an epidemic which in a short space of time attacked over 6000 subjects out of a population of 7782. Persons of all ages were stricken and almost every household was converted into a hospital. The old inhabitants who had passed through an attack as children in 1781 alone escaped. Not one old person who was exposed to the infection, and was unprotected by previous attack, failed to take the disease.

That certain individuals may exhibit a *temporary immunity* against measles is recognized by most writers. Thomas says: "I observed, during an epidemic among about 130 cases, 5 children, 2 of whom were boys of two and three years, evince an immunity during this epidemic, while 2, boys of eight and twelve years, and a girl of nine years had evinced it as well during previous ones."

Hoff makes mention of 3 men, acting as nurses in the epidemic of 1846 in the Faroe Islands, who remained exempt, but who contracted the disease when it recurred in the islands in 1875.

Spiess² states that a number of children, varying in age from four to seventeen years, after having been previously exposed to measles without contracting it, fell ill in 2 cases after seven weeks, in 1 after two months, in 4 after two and a half months, and in 1 after five months.

Moore³ reports the case of a boy who, passing through two epidemics of measles with impunity, fell ill during a third and gave the disease to a younger brother, who at the time of the first invasion was not born, but who had successfully resisted the second one.

It is difficult to explain this temporarily absent susceptibility, but it is quite analogous to that observed in suckling infants.

The presence of an acute disease is apt to temporarily diminish susceptibility to measles, or, when the infection is received, to postpone its outbreak until convalescence from the first disease. This is true of most of the exanthematous affections. The susceptibility to measles may even be temporarily abolished during the existence of another acute malady. An instance of this has recently attracted our attention.

¹ This remarkable epidemic was carefully studied and reported by Panum, who visited seventeen of the twenty islands of the group during a period of four months. A later epidemic in 1875 was assiduously investigated by E. M. Hoff; Sundhedscollegiets Aarsberetning for 1876.

² Quoted by Thomas, loc. cit.

³ Quoted by Thomas, loc. cit.

A boy, aged five years, was believed to be suffering from smallpox and was sent into the wards of the Municipal Hospital devoted to this disease. On making our rounds we discovered that the boy had measles at the height of the eruptive stage and not smallpox; he was immediately transferred to other quarters. He had been in the ward about fifteen hours; in this same ward were about fifteen children, from a few months to twelve years of age, suffering from smallpox in its various stages. Some of these children later succumbed to smallpox, but not one contracted measles.

Age.—Measles most commonly attacks individuals between the ages of one and ten years. This age incidence is determined by several factors—an almost universal vulnerability to the disease, a diminished susceptibility during the first year of life, and the immunity conferred by one attack. There can be no doubt that infants under one year of age and particularly those under six months will commonly escape measles when exposed to the disease. This is equally true of rubella, and, in a measure, true also of scarlet fever. This immunity is not absolute, but only relative. There are numerous records of infants of tender age who have contracted measles, but under six months they are very apt to resist the infection altogether.

Pfeilsticker¹ reports an interesting epidemic of measles occurring in Hagelloch, near Tübingen, in which 188 out of 197 children under fourteen years of age, contracted the disease. Seven of the children were under six months of age and *all of this number remained well*. Of 10 infants between six months and one year, 9 contracted measles. This experience would tend to show that infants under six months of age are very much more immune than those a few months older.

Lé Barbillier,² in an epidemic of measles in the Foundling Hospital at Bordeaux, noted but 7 cases among 40 children under one year of age. Mayr reports that of 10 newborn and suckling infants exposed to the disease, but 1 contracted it.

The susceptibility, then, to measles is largely in abeyance during the first six months of life; after this period it gradually increases so that after the first year the temporary immunity has entirely vanished.

Measles may in extremely rare cases be contracted during intra-uterine existence, and children may be born with fully developed eruptions. After careful search of the literature Thomas was able to find but 6 properly authenticated instances of this occurrence. Numerous authors refer to congenital measles, but the facts in many cases render the diagnosis doubtful. Several authors cited by Thomas record cases which bear the stamp of genuineness. Clarus reported to the Medical Society of Leipzig that he had seen the eruption of measles quite plainly on a foetus the mother of which had died during the exfoliative stage of the disease. Hedrich speaks of a female child born on the fourth day of an attack of measles in the mother that was covered with the measles exanthem and had catarrhal symptoms, sneezing, coughing, and inflamed

¹ Beiträge zur Pathologie der Masern, etc., Tübingen, 1863.

² Quoted by Thomas, loc. cit.

eyelids. Vogel, Guersent, Hildanus, Lidelius, Michaelson, Seidle, Ballantyne, and others have also reported cases which in all number about 20. The diagnosis in such cases could be controlled, as Thomas suggests, by noting the susceptibility or immunity of these children in later years. He reports an attack of measles in a woman five months pregnant, in which the susceptibility of the foetus was not affected, for the child contracted measles at the age of nine years.

Von Jürgensen says: "The poison must be able to pass through the placenta. It is presumed that the child becomes infected very soon after the disease organisms have attacked the mother, since the disease presents the same stage of development in mother and child at the time of the latter's birth."

Hoff, on the other hand, states that "without exception everybody born in the year 1846 whose mother, according to her own statement and as affirmed by comparison with the church records, contracted measles during pregnancy, was attacked by the disease, if exposed to it, at the time of the epidemic of 1875." Hoff states that this was true no matter what month of pregnancy the mother happened to be in when she was suffering from the measles. This experience throws a flood of light upon the question of the placental transmission of measles. Hoff draws therefrom the conclusion that "there is not the slightest ground for believing the contagion to be carried to the foetus through the placental circulation."

Adult life offers no such immunity against measles as is commonly observed toward scarlet fever. Those who escape measles in childhood do not fail to take the disease when exposed in later years. Measles in adults is comparatively uncommon only because most persons have suffered an attack in childhood. Gregory states that measles was absent from the island of Madeira for twenty-five years; when, in 1808, it did invade the island, it found almost the whole population susceptible, and in four months destroyed 700 lives.

Panum states that in the epidemic of measles in the Faroe Island in 1846 not one person who had escaped measles in the epidemic of 1791 remained free of the disease. It is evident that all of these persons must have been over fifty years old. Measles may even attack persons in the decrepitude of old age. Drake¹ in 1844 observed several cases in negroes of advanced age, one of them at least eighty years old. Heim saw a woman of seventy-six years with measles, and Michaelson reports a case in a patient eighty-three years old.

Measles is undoubtedly the most common of all of the exanthematous diseases. Owing to its extremely contagious character epidemics are far more extensive and widespread than those of scarlet fever. While large cities are subject to epidemic outbreaks from time to time, the disease seldom dies out altogether. In great centres of population the disease may be said to be endemic, sporadic cases developing every now and then. When the increase in population by births or other

¹ Drake, Heim, and Michaelson, all cited by Thomas, *loc. cit.*, p. 48.

causes creates a sufficient number of unprotected subjects the infection takes hold and an epidemic results. Thomas asserts that in large communities epidemics may be expected about every two or four years. In small towns and villages the interval of freedom is much longer.

Whitelegge,¹ from a careful study of English statistics, estimates that epidemics of measles appear about every two years. About every ten years an epidemic of considerable severity with high death rate may be expected.

In localities isolated by geographical position, such as islands in the ocean, communities may remain free from measles infection for decades, a half-century, or for even a longer period. Gregory, writing in 1843, says, "Australia and Van Diemen's Land are to this day exempt from measles." When the disease is once introduced into such isolated communities, it finds almost the entire population susceptible and smites with the hand of a plague. It has already been mentioned that in the Faroe Islands, which had been free of measles for sixty-five years until 1846, 6000 out of a population of less than 8000 were attacked.

Measles may, from time to time, cover so extensive a territory as to become *pandemic*, in the same manner as smallpox, particularly before the days of vaccination. At such times an entire country, or, indeed, several countries may be attacked. Hirsch mentions a number of such general outbreaks during the century just passed. In 1796-1801 measles was present in a large part of England and France; in 1823-24 it prevailed extensively in Germany, and in 1826-28 in the Netherlands and Germany. In the two years from 1834 to 1836 it swept over the greater part of northern and middle Europe. An extensive epidemic prevailed in 1846-47 in both the new and the old hemispheres. Since the days of rapid transoceanic travel it is quite easy for diseases like measles and smallpox to be contracted on one side of the ocean and to develop on the other. Infectious diseases follow the channels of travel. Measles is not apt to be carried by infected baggage or clothing, but by the breeding disease in an exposed and unprotected person.

Season.—According to Gregory it was formerly believed that measles began in January, reached its crisis at the vernal equinox, and ceased in the summer solstice. Gregory dissents from this view and states that "the recurrence and duration of epidemics are, in Europe, wholly irrespective of season. In Bengal, however, measles never originates except in the cold season. Season affects, too, there the character of the symptoms. In the hot months the eruption is more vivid and more elevated, and the internal organs comparatively but little affected. In the cold season the affection of the mucous tissues is best developed."

Hirsch's figures show that while measles most commonly occurs during the winter months, no season of the year is entirely exempt.

Three hundred and nine epidemics collated by Hirsch began in the following months:

¹ British Medical Journal, 1893, vol. i. p. 541.

THREE HUNDRED AND NINE EPIDEMICS OF MEASLES CLASSIFIED ACCORDING TO SEASON (HIRSCH).

December	28	June	19
January	64	July	16
February	14	August	8
Winter, 96 epidemics.		Summer, 43 epidemics.	
March	43	September	16
April	28	October	24
May	23	November	28
Spring, 94 epidemics.		Autumn, 76 epidemics.	

Thomas suggests that the lessened incidence of measles in mild weather may be, in part, due to the better ventilation of sick-chambers and the consequent diminished concentration of the infection. In cities a much more important cause of the falling off of measles in hot weather is the closing of the schools. All of the exanthematous diseases in large communities diminish during the school vacations and increase upon resumption of the sessions in the fall. There can be no doubt that the close contact of children in the schools is a fertile cause of the spread of the various contagious diseases.

Contagious Period.—The contagious period of measles may, in general terms, be said to last from the beginning of the prodromal stage to the complete disappearance of the eruption. That measles can be communicated before the appearance of the eruption is generally admitted by writers, and is borne out by observation.

Panum¹ details the history of a case in the Faroe Islands in which a young man had slept in a bed with an infected patient "several days" before the rash broke out; fourteen days later the eruption of measles appeared upon him. Hoff reports an equally conclusive instance in the case of a clerk infected at Thorshavn.

Eyre² reports an interesting and apparently conclusive instance of pre-eruptive contagion. A schoolmaster at Beckenham returned to his school on April 30, 1888, at the end of the Easter holidays; he did not feel well, but continued his work on May 1 and 2. He went to bed on the evening of May 2, and during the night the eruption appeared. Although the students were sent away, all of the susceptible ones—fourteen in number—contracted the disease.

Ransom³ collected five instances of measles infection conveyed before the appearance of the rash. In two of these cases the disease was communicated two days before the eruption. In a case seen by Croskey,⁴ the infection was believed to have been transmitted four days before the appearance of the rash. Holt reports a similar case occurring in the Babies' Hospital in which the disease was conveyed four days before the eruption appeared. On the other hand, one of Ransom's cases failed to give the disease to seven susceptible children exposed three days before the eruption appeared.

Measles is *most contagious* at the height of the eruption. Indeed,

¹ Virchow's Archiv, vol. i p. 499.

² British Medical Journal, January, 1877.

³ British Medical Journal, February 23, 1899.

⁴ Quoted by Ransom, loc. cit.

some writers contend that the communication of contagion is limited to the eruptive stage. This is the opinion of Hoff, who had a splendid opportunity of studying the Faroe Islands cases. Panum says it is uncertain whether the catarrhal and desquamative stages are contagious. Peterson, a colleague of Hoff, concedes that the catarrhal period may be contagious, but denies that this extends to the stage of desquamation.

We have on several occasions had children brought into the wards of the Municipal Hospital with the stains of the measles exanthem still visible; although in each of these instances a score of children were freely exposed, many of whom were unprotected by previous attack, no cases of measles developed among them.

There can be no doubt that the contagiousness of measles is distinctly diminished during the stage of desquamation. We would be extremely loath to assert, however, that it is abolished at this time, and we would certainly not act upon the assumption that it is. In the absence of adequate and conclusive data upon this point it is advisable to isolate measles patients until the completion of desquamation, or, at any rate, for a period of three weeks from the commencement of the disease.

Second Attacks.—One attack of measles nearly always confers immunity against subsequent attacks. It is generally admitted by careful and experienced observers that second attacks are extremely rare. The infrequency of this occurrence may be appreciated when it is stated that Maizelis¹ was able to find only 106 instances of multiple attacks in the entire literature of the subject. Of these 103 were second attacks and 3 were alleged to be third attacks. This is an exceedingly small number, even admitting many unpublished cases, when the universal extent of measles is considered.

Panum, who saw 6000 cases in persons of all ages in the Faroe Islands epidemic, did not observe one instance of second attack. Rosenstein, in an experience extending over forty years, met with but a single instance of the recurrence of measles. Willan, in a rich experience of twenty years, did not see one case. Camby could not recall one instance of relapse or recurrence among 700 cases of measles. Thomas' large experience did not include a case and the same may be said of the authorities quoted by him—Berndt, Theussink, Schönlein, Mayr, Schott, and Bartscher. While the experience of these eminent physicians indicates the great infrequency of second attacks, a sufficient number of cases has been reported to prove their occasional occurrence.

Recurrences may take place a few days to a few weeks after the first attack, in which event one might properly speak of a *relapse*, or they may take place months or years later, constituting true *second attacks*. Relapses have been reported by a considerable number of observers.²

¹ Ueber die durch das Ueberstehen von Infectiouskrankheiten Immunität, Virchow's Archiv, vol. cxxxvii. p. 468.

² Among those who have reported relapses of measles may be mentioned Van Diezen, Battersey, Robédière, Flemming, de Haen, Haartman, Webster, Kassowitz, Stiebel, Brunzlow, Lulthlen, Mauthner, Klerulf, Trojanowsky, Home, Lewin, Gauster, Karg, Böhler, Tresling, Spiess, Feltz, Lemoine, Vergeley, Fischer, Roger, and others.

The chapter on the history of the book is a very interesting one. It shows how the book has been used by different generations of students and how it has been adapted to different needs. The author also discusses the book's influence on the development of the subject.

The book is a very good one. It is well written and easy to read. It contains a lot of interesting information and is a very good reference work. I highly recommend it to all students of the subject.

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¹ See, for example, p. 10.

² See, for example, p. 10.

³ See, for example, p. 10.

⁴ See, for example, p. 10.

⁵ See, for example, p. 10.

developed a discharging nose and congested and watery eyes. On the fifth day the animal was sick, had a temperature of 103° F., shivered, and refused food. On the eighth day the non-hairy portions of the face showed red spots, which spread in another day over the body, being followed by a mild desquamation. Two pigs that had been exposed to the first one developed similar symptoms in the course of two weeks. The attendant regarded the disease as swine fever, but examination of the blood and mucus failed to show the presence of the bacillus found in this disease.

Josias¹ failed to confirm the results obtained by Behla, but succeeded in communicating the disease to monkeys. Chavigny² also observed measles in a monkey.

THE SYMPTOMATOLOGY OF MEASLES.

Incubation Period.—The incubation stage of measles may be said to be the period elapsing between the date of infection, which, in most cases, is the time of initial exposure and the development of febrile symptoms. In the majority of cases this stage is in the neighborhood of ten days; the eruption usually appears on or about the fourteenth day. It is only possible to accurately determine the duration of the incubation stage in cases in which the exposure has been but once and for a brief period.

While persons susceptible to measles will ordinarily take the disease upon first contact, this is not invariably the case. Where there has been prolonged exposure it is not possible to accurately fix the time of infection.

Some writers speak of the incubation period of measles as about fourteen days. In such a statement there is either an inaccuracy of time or terms. The incubation period ceases when the usual symptoms of measles manifest themselves. While there is a decided variability in the duration of the symptoms preceding the eruption, we are not justified in speaking of the incubation period as extending to the appearance of the eruption.

In general terms it may be said that the incubation stage of measles is about *ten or eleven* days. The period from exposure to the development of the rash is about fourteen days. The incubation period in this disease is subject to less variation than in scarlet fever, rubella, or chicken-pox. Panum had a splendid opportunity of studying the incubation period in the Faroe Islands epidemic. He reports about 40 cases, in all of which the period to the appearance of the rash was thirteen or fourteen days. The facts in these cases are thoroughly reliable, the date of exposure having been accurately determined in each. Smith and Dabney³ report an outbreak of measles in an institution in Virginia, in which the disease developed in twenty children just eleven days after the rash appeared in the first patient. Spiess⁴ estimated the time elapsing between the appearance of eruptions in the infecting and

¹ *La méd. mod.*, 1898, No. 29.

² Quoted by Holt, loc. cit.

³ *Bull. méd. de Paris*, 1898, xii. p. 334.

⁴ Cited by Thomas, loc. cit.

infected patients in 147 cases. In 117 cases the interval was between ten and fourteen days, in 8 cases it was nine days, and in 22 cases it was between fifteen and eighteen days. Salzman¹ found the interval between the eruptions in 25 cases infected from a single patient to be as follows: In 3 cases it was nine days, in 8 cases ten days, in 13 cases eleven days, and in 1 case twelve days.

Holt² has collected a series of 144 cases, of which 25 were his own, in which the incubation period could be traced definitely. The periods were as follows: Incubation of less than nine days, 3 cases; incubation of nine or ten days, 22 cases; incubation of eleven to fourteen days, 15 cases; incubation of fifteen to seventeen days, 19 cases; incubation of eighteen to twenty days, 5 cases.

In 66 per cent. of the cases the incubation was between eleven and fourteen days, and in but 1 case was it under a week. There have been cases in which the incubation period has been but five days, but such instances must be exceedingly rare. On the other hand, unusually long periods are on record. Roux³ observed an epidemic of measles that developed among a number of people on shipboard after the vessel was seventeen days out of port; no case of measles had previously existed among those on board.

While it is seen that some variability exists in the incubation period of measles, it will be found in the majority of cases to be in the neighborhood of ten or eleven days.

While the incubation stage is generally devoid of symptoms, patients occasionally feel unwell and complain of lassitude, headache, malaise, etc., during the latter part of the period. Gregory says: "Sometimes the entire incubation stage is marked by languor, lassitude, and a sense of malaise and occasionally a characteristic symptom such as cough."

Prodromal or Invasive Period.—In those cases in which the latter days of the incubation period are marked by mild constitutional disturbances the invasive stage comes on insidiously. It is rather uncommon for measles to be ushered in abruptly with high fever. The onset is more gradual and characterized by less intensity than that of scarlet fever. Convulsions and vomiting are rare occurrences. The mucous membranes are early attacked, giving rise to symptoms which have caused this period to be known as the catarrhal stage. The eyes are reddened and watery, sensitive to light, and often show puffiness of the lids. The nose at first feels obstructed, but soon a discharge issues therefrom, accompanied by repeated sneezing. Occasionally nose-bleed occurs, but this is seldom severe. In pronounced cases the face may present a puffy and swollen appearance. The involvement of the larynx and trachea gives rise to hoarseness and to a dry, hard, and high-pitched cough. At times the throat is sore, exhibiting upon inspection redness and swelling of the tonsils, soft palate, and pharynx. The constitutional symptoms consist of fever, headache, loss of appetite, drowsiness, and irritability. Somnolence is often a prominent feature. Chills are rare,

¹ Cited by Thomas, *loc. cit.*

² *Diseases of Infancy and Childhood*, New York, 1899, p. 911.

³ Quoted by Thomas, *loc. cit.*

PLATE XLVII.

Fig. 1



Fig. 2



Fig. 3.



Fig. 4



The Pathognomonic Sign of Measles (Koplik's Spots)

Fig. 1.—The discrete measles spots on the buccal or labial mucous membrane showing the isolated rose-red spot with its minute bluish-white center on the normally colored mucous membrane.

Fig. 2.—Shows the partially diffuse eruption on the mucous membrane of the cheeks and lips: patches of pale pink interspersed among rose-red patches, the latter showing numerous minute white spots.

Fig. 3.—The buccal mucous membrane when the measles spots completely confluent and give a diffuse redness with the myriads of bluish-white specks. The exanthema on the skin at this time generally fully developed.

Fig. 4.—A diffusion does not denote a mistake for measles spots. Mucous membrane normal in color. Minute bluish-white spots are not supplied by a red area. Always discrete.

occurring, according to Ziemssen and Krabler, only five times in 311 cases studied by them. The bowels are usually constipated, although occasionally a slight diarrhoea is observed.

The *fever* does not observe any set standard, but is subject to considerable variation. In some cases it rises rapidly during the first twenty-four hours, reaching by evening 102° to 103° F. On the morning of the second day, or occasionally the third, the temperature may decline to normal or thereabouts, accompanied by an improvement in all of the symptoms. After this remission the temperature again begins to rise, usually on the evening of the third day, continuing its ascent on the fourth day, with the appearance of the eruption. In other cases the fever is very moderate at the outset, not exceeding 101° F. A gradual increase in the temperature and in the catarrhal symptoms occurs up to the appearance of the rash. In some epidemics the prodromal symptoms are so mild as to escape the observation of the parents of the patient, who then assert the eruption to be the first symptom. On the other hand, there are epidemics in which measles develops abruptly with high fever in such a manner as to disguise the oncoming disease until the appearance of the rash solves the diagnosis.

In the average case of measles the invasive period lasts about four days; there are, however, numerous exceptions to this duration, particularly in infants. Holt made notes of the duration of the invasive stage in 270 cases. His figures are appended:

One day or less . . .	35 cases.	Six days . . .	20 cases.
Two days . . .	47 "	Seven days . . .	6 "
Three days . . .	64 "	Eight days . . .	2 "
Four days . . .	64 "	Nine days . . .	2 "
Five days . . .	29 "	Ten days . . .	1 case.

Enanthem, or Mucous-membrane Eruption.—It is a proved observation that the eruption of measles may be seen on the mucous membrane of the mouth in advance of its appearance on the cutaneous surface. Commonly, on the second day, inspection of the mouth will disclose the presence of an enanthem. The presence of a mucous-membrane eruption was recognized by physicians in the early part of the nineteenth century, as is evidenced by the writings of Willan, Heim, and others. Most of these and later observers have described the enanthem as consisting of dark-red or light-red spots.

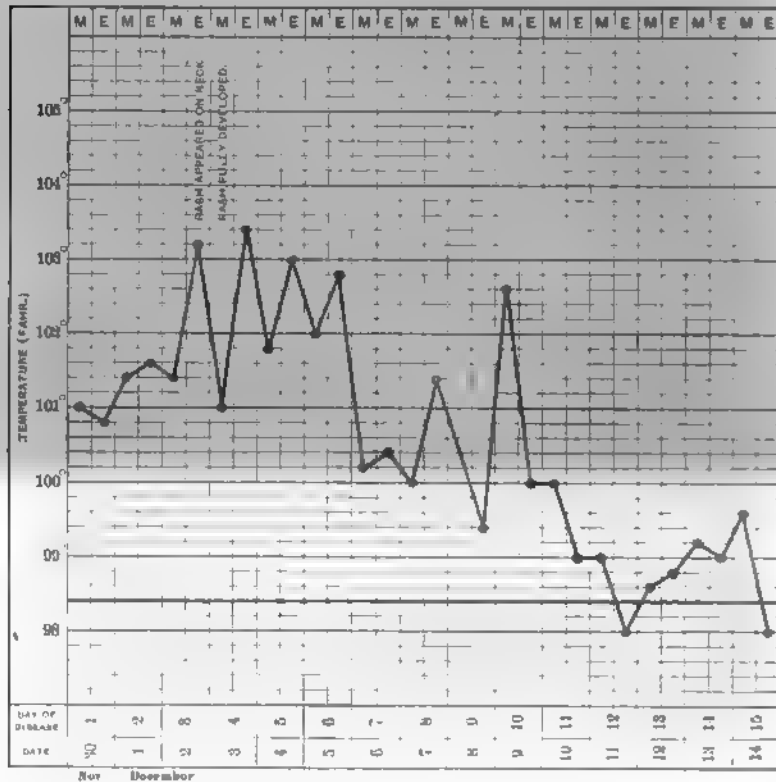
Flindt¹ in 1880 described the enanthem of measles in a most accurate and detailed manner. He says: "The eruption consists of round or somewhat irregularly shaped, light-red spots, not very distinctly circumscribed, and only just raised above the level of the mucous surface. The spots vary in size from a pinhead to a lentil, are in part isolated and in part collected into groups, quite irregular in shape, and, in some places, coalescent. At the centre of the small red spots, and giving them a peculiar appearance, are situated numbers of tiny, whitish, shiny, raised points, apparently vesicular in character and irregularly grouped according to the arrangement of the spots on which they lie. These tiny

¹ Reports of the Danish Board of Health, translated and cited by von Jürgensen.

miliary vesicles can be both seen and felt as distinct elevations. The palpebral conjunctiva is reddened throughout, and besides the net-like injection dependent on the distribution of its blood supply it sometimes appears spotted and covered with miliary, pearl-covered, raised points, similar to those on the mucous membrane of the palate.

"Similar groups of spots and vesicles can now also be perceived on the mucous membrane of the cheeks, especially on the parts corresponding to the space between the upper and lower molar teeth."

FIG. 79



A case of measles in a child three and one-half years of age, developing in the Municipal Hospital, temperature record from the first day of illness.

The measles enanthem has been carefully studied in recent years by Filatow (1895), Canby (1895), and Koplik (1896). The last-named physician¹ describes the mucous-membrane eruption as follows: "If we look in the mouth at this period (invasion) we see a redness of the fauces; perhaps, not in all cases, a few spots on the soft palate. On the buccal mucous membrane and inside of the lips we invariably see a distinct eruption which consists of small, irregular spots of a bright-

¹ Archives of Pediatrics, December, 1896, vol. xiii, and Medical Record, New York, 1896.

PLATE XLVIII.



Patient with Measles Exhibiting Eruption and Catarrhal
Inflammation of the Eyes.

red color. *In the centre of each spot* there is noted, in strong daylight, a *minute, bluish-white speck*. These red spots with accompanying specks of a bluish-white color are absolutely pathognomonic of beginning measles, and when seen can be relied upon as a forerunner of the eruption. No one has to my knowledge called attention to the pathognomonic nature of these small, bluish-white spots. Sometimes only a few red spots with this central bluish point may exist—six or more; in marked cases they may cover the whole inside of the buccal mucous membrane.

“The eruption just described is of greatest value at the very outset of the disease, the invasion. As the skin eruption begins to appear and spreads, the eruption on the mucous membrane becomes diffuse and the characters of a discrete eruption disappear and lose themselves in an intense general redness. When the skin eruption is at the efflorescence the eruption on the buccal mucous membrane has lost the character of a discrete spotting and has become a diffuse red background, with innumerable bluish-white specks scattered on its surface. The mucous membrane retrogrades to the normal appearance long before the eruption on the skin has disappeared.”

Koplik also speaks of irregularly shaped, rose-colored spots and streaks which are commonly seen on the hard and soft palate and also on the cheeks. They present small, whitish, punctate, miliary vesicles. Koplik states that the rose-colored papules or streaks with superimposed miliary vesicles are found in rōtheln, scarlet fever, and some cases of simple angina, but the reddish spots with bluish-white specks in their centres occur only in measles.

Subsequent observations have confirmed the claims as to the pathognomonic nature of these spots. They do not appear to be present in any other disease. We have examined the mouth in many cases of rubella and have noted the presence of red spots similar in appearance to those seen on the skin, but we have never seen such spots surmounted by bluish-white specks as occur in measles.

Filatow speaks of a desquamation of the epithelium of the mucous membrane of the lips and cheeks in the form of whitish shreds.

Baginsky noted desquamation on the gums in the form of whitish patches and thought this appearance to be characteristic of measles. We have repeatedly noted the presence of these whitish patches on the gums in scarlet fever.

The presence of the measles enanthem is of great diagnostic value; its absence has a less important negative evidence because in a small proportion of measles cases the spots are not present. We have seen a small proportion of cases of measles in which the Koplik spots were absent. Of 187 cases of measles examined by Cotter¹ at the New York Foundling Hospital, 169 showed the characteristic spots. In 8 patients the spots were absent, while in 10 patients their presence was doubtful. In 78 cases the spots appeared synchronously with the cutaneous

¹ Archives of Pediatrics, 1900, xvii.

eruption; in 88 cases the spots preceded the eruption by one to five days; in 2 cases the spots did not appear until after the rash.

Lorand¹ studied the incidence of Koplik's spots in two series of cases of measles, numbering in all 523. The spots were absent in 30 cases out of this number.

Pre-eruptive Rashes in Measles.—In almost all of the exanthematous fevers the true specific eruptions may be preceded by accidental rashes. Measles is no exception, although prodromal erythematata in this disease are rare.

Meredith Richards² says: "In the pre-eruptive stage of measles there may be a scarlatiniform rash, usually more transient and more diffuse than the eruption of scarlatina. This rash is responsible for some of the cases in which measles is diagnosed as scarlet fever. Another pre-eruptive accidental rash is a somewhat faint general erythema, not unlike the true measles eruption in its general appearance, but almost confined to the trunk and limbs, and more diffuse and less distinctly papular.

Roger³ records 5 cases of prerubeolic erythema occurring among 1917 cases of measles. These developed in an infant of fourteen months, a child of three years, and three adults, and appeared two or three days before the time of the measles eruption. We recall a young girl, aged fourteen years, in whom a partial scarlatiniform erythema of considerable intensity developed upon the neck, face, and upper part of the chest on the second day of the febrile symptoms. The symptoms suggested at first an atypical scarlatina. The rash disappeared, however, in about thirty-six hours, and twelve hours later, on the fourth day of the illness, the eruption of measles appeared. Gerhardt⁴ observed a prodromal exanthem in the femoral triangle which appeared a day before the measles eruption. Comby⁵ records 2 cases of pre-eruptive rashes. A girl, aged four and a half years, developed at the beginning of the invasive stage of measles a scarlatiniform eruption which persisted throughout the 18th and 19th of July, the true measles exanthem appearing on July 22d. Another child of the same age was admitted to the hospital on July 20th with a morbilliform rash; on July 22d the measles eruption appeared.

The cause of these accidental rashes cannot be readily assigned. In most of Roger's cases the rashes were morbilliform; it is possible that these represent abortive attempts of the true eruption to appear before the usual time. Thomas says: "The earliest signs of the eruption, at first in a thoroughly undeveloped condition, appear not infrequently upon the first day of the febrile period, more often on the second or third." The scarlatiniform rash, whatever may be the cause, is of importance because of errors of diagnosis which its presence may occasion.

¹ *Jahrbuch f. Kinderheilk.*, 1901, III. p. 658.

² *Accidental Rashes Occurring in the Course of the Exanthematata*, Quarterly Medical Journal 1898, vol. v. p. 31.

³ *Les maladies infectieuses*, Paris, 1902, p. 574.

⁴ Quoted by Thomas.

⁵ *Traité des maladies d'enfance*, Paris, 1897.

PLATE XLIX.



Eruption of Measles beginning as Closely Aggregated
Small Papules.

The Eruptive Period.—The measles exanthem usually appears upon the fourth day of the febrile disorder. It does not invariably appear in one particular locality, as some writers state. The most common initial sites are the side of neck, the mastoid region of the temples and frontal border of hair, the cheeks, and the chin—in other words, about the face and neck. The eruption of measles has a special predilection for the face, which is earlier and more copiously covered than other areas.

It is not uncommon for the eruption in this region to become confluent and to give rise to a dusky turgescence of the skin. From the face and neck the rash rapidly extends over the trunk and upper extremities. The lower extremities are the last and least intensely attacked; commonly but a few scattered lesions are seen upon the legs.

Aitken¹ describes the measles eruption as appearing in three crops. The first crop appears on the face, neck, and upper extremities, on the third or fourth day of the disease; on the following day the second crop covers the trunk, and on the third day the third crop appears on the lower extremities.

Character of the Eruption.—The essential lesion of measles is a slightly elevated macule; it is sufficiently elevated to be recognized both by the sense of sight and touch. The more circumscribed the lesion is the more is it distinctly papular, and the more diffuse and confluent the eruption is the more does it approach an erythematous and un-elevated efflorescence. The macules vary greatly in size from a pin-head to a bean or finger-nail. They are irregular in outline, being at times rounded or oval, but at other times angular, indented, and spun out. They are usually sharply margined and stand out sharply against the pale, integumentary background.

To the fingers passed over the lesions a soft or velvety feel is imparted, quite unlike the indurated feel of the early smallpox eruption. The color of the measles exanthem varies in different patients and at different stages in the same individual. It is seldom as vivid a red as is seen in the exanthem of scarlatina. The macules in the beginning have commonly been compared with the appearance of flea-bites; they are of a dull-red color, not infrequently becoming dusky. In some patients the eruption, particularly when it becomes confluent, has a distinct bluish tinge. The bluish coloration is not at all uncommon upon dependent areas such as the back. In pronounced cases, particularly in adults, the face may exhibit an extremely dusky-red appearance, which, with a slight swelling of the skin, produces a strange and disfiguring turgescence.

On the first day of the eruption the lesions are small and discrete, in many cases bearing a resemblance to the eruption of rubella. The macules subsequently enlarge in size and in number, coalesce in areas, and produce a rash which is essentially blotchy. The arrangement of the measles lesions lacks symmetry and uniformity. At times distinct

¹ The Science and Practice of Medicine, 1868, p. 288.

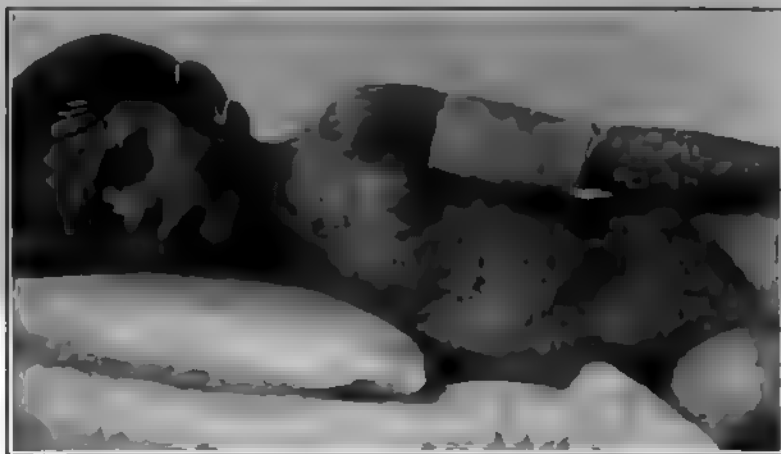
crescents and segments of circles can be distinguished; at other times such configurations are absent. The rash of measles does not invariably consist of slightly elevated, velvety macules. There are at times distinct papules present, and miliary vesicles are not infrequently seen.

Mayr, in his article on "Measles" in Hebra's *Diseases of the Skin* (1866), distinguishes a number of varieties of measles based upon the character of the eruption. The term *morbilli leves* is applied to the common form in which the character of the eruption is smooth and flat, the individual macules being separated by areas of healthy skin.

In *morbilli papulosi* there appear dark-red or reddish-brown points or papules, the size of millet or hemp seed, situated at the mouths of hair follicles. This form of measles is said to occur in certain epidemics, taking the place of the more usual variety.

We have known the papular form to be confounded with smallpox on more than one occasion.

FIG 80



Measles exanthem on the third day of the eruption and the seventh day of the disease.

In *morbilli vesiculosi* or *miliares* small pinpoint to pinhead-sized vesicles are seen upon the summits of the lesions. This gives the skin an appearance resembling prickly heat, and, indeed, the presence of the miliary vesicles has been ascribed to the sweating process. This is probably not the case, as the vesicles are identical with those commonly seen in scarlet fever, in which disease the sweating process is in abeyance.

Morbilli confluentes describes the form in which the macules run together and become confluent. It will be remembered that this was the term applied to scarlatina before the days of Sydenham.

We have seen numerous cases which justify the use of the term confluent measles. We recall a very severe epidemic of measles which prevailed in the scarlet-fever wards of the Municipal Hospital a few winters ago. The eruption in these cases was normal in the beginning, but in a few days became intensely confluent and vivid over the greater

PLATE I.



Pronounced Measles Eruption on Sixth Day of the Disease.
Tendency to confluence of the eruption especially upon the thighs.

part of the cutaneous surface. The resemblance of the rash after a few days to that of scarlet fever was striking, although in most every instance there could be found in one region or other, and commonly about the buttocks, pale areas of skin against which the marginate border of the confluent rash stood out in sharp contrast. The mortality among these patients was very high.

Morbilli hemorrhagici is that variety in which the macules are purplish or bluish and from which the color cannot be made to disappear by the pressure of the fingers. This condition is usually observed in malignant cases.

The various lesions here described may be seen to a certain extent in ordinary cases, but the form characterized by papules, miliary vesicles, or confluence may each be particularly well pronounced in certain epidemics.

As regards the rapidity of extension of the measles eruption, Thomas observes that if it appears early in the invasive stage it is apt to remain in a moderately developed condition for several days upon the face alone. A more rapid evolution and spread occur when the temperature begins to rise sharply. On the other hand, when the exanthem first appears at a late period, when the fever is reaching the acme, the rash spreads rapidly over the body. The intensity of the eruption and the degree of the fever increase *pari passu*. At the beginning of the eruption the temperature does not register its maximum; it is only after the full development of the exanthem that the pyrexial fastigium is reached. The temperature at this time is commonly 104° F., and not infrequently 105° F. The fever may reach even a higher degree than this. Temperatures of 108° and 109° F. have been observed, and Hunter¹ saw a child of sixteen months with a temperature of 110° F., the patient ultimately recovering. When the maximum fever is attained the eruption is copious and intense; the face is often of a uniform dusky-red color and œdematous, particularly about the eyelids. The entire body is, as a rule, covered, not even the palms and soles being exempted. Not infrequently the rash gives rise to a considerable degree of itching.

During the development of the eruption, the local as well as the constitutional symptoms increase in intensity. The conjunctivæ are red and swollen and an abundant mucopurulent discharge issues from the palpebral cleft, later drying and gluing the lids shut. When the lids are open there is great sensitiveness to light. A similar profuse discharge from the nose irritates and excoriates the nostrils and upper lip. There is commonly painful swallowing and enlargement of the glands at the angles of the jaw. The cough is frequent and harassing, and the voice hoarse and aphonic. Evidences of bronchitis are usually present at this time. The ear placed to the chest will discover the presence of dry and moist rales. In large children and adults there is expectoration of mucopurulent material. Children are much prostrated, manifest great thirst, refuse food, and are either extremely restless and peevish or

¹ British Medical Journal, April, 1898.

somnolent. Vomiting and abdominal pain are uncommon, but diarrhoea is frequent, the stools being offensive and often slimy. The eruptive stage lasts ordinarily four or five days. With the fading of the rash there is a gradual subsidence of the fever and the catarrhal symptoms. It is rare for a critical fall of temperature with sweating to occur. When this does take place there is apt to be alarming prostration. The decline of the fever is by steps, but is nevertheless moderately rapid. Ordinarily but twenty-four to thirty-six hours elapse between the acme of the fever and the return to normal. When the decline is slower than this it is characterized by morning remissions and evening exacerbations. During convalescence the temperature may, for several days, be below the normal line.

As the rash fades, the appetite improves, somnolence and irritability disappear, and the child begins to acquire its normal brightness, and desires to leave the bed. The inflammation about the eyelids and the mucous discharges gradually improve, although the eyes may remain sensitive to light for some days. The hoarseness and cough persist for some time, but in favorable cases improve from day to day. Where no bronchial or pulmonary complications develop the patient is practically well at the end of ten days or two weeks, but, of course, requires to be carefully guarded against exposure.

Stains (Pigmentation).—As the rash disappears there are left on the skin faint reddish-brown stains which may be detected for a number of days. The stains correspond with the size and shape of the original lesions and are highly characteristic; they are of considerable diagnostic value, and will often enable one to diagnose an attack of measles after it has subsided. When children presenting the stains of the measles exanthem are admitted into a hospital or other institution, they should be isolated in order that they do not transmit the disease to others. The stains may persist for a week or even longer.

Hemorrhagic Eruption in Measles of Moderate Severity.—It is not rare for the eruption in cases of measles of average severity to exhibit hemorrhagic extravasation into the skin. The macules in such cases are of a deeper hue, varying from a claret red to a reddish-blue tint. It is observed that the spots do not disappear upon pressure of the fingers. The hemorrhage into the skin may be noticed at the height of the eruption, or it may become evident only during the decline, when the redness begins to fade. Claret-color or bluish discolorations are left which pass through the color variations observed in an ordinary bruise. The discolorations coincide in size and shape with the original measles spots.

It is important to distinguish this benign form of hemorrhagic eruption from the malignant variety. In the former the constitutional symptoms are not unusually severe and hemorrhages do not take place from the various mucous membranes. We have not infrequently noted hemorrhagic measles spots in cases of average severity, which pursued a favorable course, terminating in recovery. Holt observed hemorrhagic eruptions in about 5 per cent. of his cases.

Desquamation begins as the rash fades away and is first noted upon initial sites of the eruption, namely, the face and the neck. The scaling is branny and furfuraceous, and is often so fine as to require careful scrutiny to observe it. The skin seldom comes off in large flakes as it does in scarlet fever. The amount of desquamation varies in different cases and is usually proportionate to the intensity of the antecedent eruption. In many patients no desquamation will be seen at all. On the trunk the perspiration which is common in measles obscures the fine scales or enables them to cling to the body linen. The desquamation is usually most observable on the face. Scaling continues ordinarily from a few days to a week, but may rarely be protracted for ten days or two weeks.

Anomalous Cases of Measles.—All exanthematous diseases exhibit at times variations from what might be regarded as the normal standard. Anomalous cases of measles may develop individually during the course of a normal epidemic, or there may be special aberrant features peculiar to prevailing forms of the disease. The special predominance of the papular element of the eruption is more common in certain epidemics. Mayr says that the Nirilas or “Nirles of Alibert” was mostly probably a papular form of measles.

The chief deviations from the normal type are those forms that exhibit unusual benignity or exaggerated severity.

Mild Measles.—In rare cases there may be an absence of one or several of the important manifestations of the disease that go to make up the characteristic symptom-complex. Thus, measles may exist without fever, without catarrhal symptoms, or, indeed, without an eruption.

Measles Without Fever (*Morbilli sine febre*), *Morbilli Apyretica*.—Leube says: “Although there may be very little fever in mild cases, it is never entirely absent.” Nevertheless, von Jürgensen¹ reports two cases of measles occurring in infants of four weeks and twenty-one months of age, respectively, who had catarrhal symptoms and undoubted eruptions, and who had been exposed to measles, who never had any elevation beyond 99° F. Extremely mild and abortive cases of measles appear to be more common in young infants, who, as has been stated, possess only a very limited susceptibility to the disease.

Measles Without Catarrhal Symptoms (*Morbilli sine catarrho*).—The absence of catarrhal symptoms is occasionally noted in infants during the prevalence of measles of the ordinary type. In such cases there is usually very little elevation of temperature and the eruption is not intense. The genuineness of these attacks is established not only by previous exposure to regular measles, but by the immunity conferred against subsequent attacks. It is evident that when the fever and catarrhal symptoms are insignificant the case must present considerable resemblance to rubella. If a disease prevails epidemically, in which these two groups of symptoms are uniformly in abeyance, the strong probabilities are that the disease is rubella and not measles.

¹ Loc. cit., p. 267.

Measles Without Eruption (*Morbilli sine exanthemate, Morbilli sine morbillis*).—As is the case in smallpox and scarlet fever, it is possible for measles to occur without the development of the exanthem. Such cases are, of course, excessively rare, but are recognized by careful and conservative writers. Thomas says that the diagnosis is more often made than is justified, but remarks that "this form of the disease may be diagnosticated in persons previously unattacked, if in a single case, during an epidemic of measles, the characteristic mucous membrane symptoms together with fever appear and become exactly as much developed as in measles with an exanthem, so that we have ground for assuming that this symptom alone is lacking from a normal course." Cases may occur in which the attack of measles is typical up to the eruptive stage, but at this point the anticipated exanthem fails to appear and convalescence is established. Embden¹ claims to have observed 20 patients among 461 cases of measles in Heidelberg, in whom the eruption was absent. The cases were of a mild type, but some few had severe complications.

Rush makes mention of persons who in 1789 presented the usual manifestations of measles, fever, cough, etc., but no eruption except in some cases a trifling efflorescence about the neck and breast. Webster² claims to have seen similar cases in 1773 and 1783.

Well-authenticated cases of this kind are said to have been seen in an epidemic in Paris in 1850. The usual premonitory symptoms of measles appeared in a number of children; the regular course was followed in a certain proportion, but in a number of others some presenting unequivocal spots of measles on the neck and chest, which rapidly disappeared, the lungs became quickly involved.³

Rilliet⁴ reports a case of severe measles without eruption in a twenty-one-month-old child who contracted the disease twelve days after other cases in the same family. There were fever, coughing, and sneezing, but the eruption did not appear. On the fourth day a lobular pneumonia developed, the child succumbing on the eighth day. Some authors accept the statement that desquamation may occur in measles without eruption. We contend, as in the case of scarlet fever, that desquamation does not occur without some antecedent structural change in the skin, and that when desquamation occurs it signifies that a rash has existed which was unobserved.

There are *mild* cases of measles in which all of the usual phenomena are present, but in an extremely moderate, and sometimes imperfect, degree. The maximum temperature in such cases does not exceed 102° F. and the fever lasts but four or five days. The eruption is faint, poorly marked, of short duration, and often so indefinite as to require other evidence to establish the diagnosis. The catarrhal symptoms are also slight, but present more uniformity than the cutaneous manifesta-

¹ Quoted by von Jürgensen, loc. cit.

² Quoted in editor's notes in Bulkley's American edition of Gregory's Lectures, 1861.

³ London Medical Gazette, June, 1850, p. 572, cited by Bulkley, loc. cit.

⁴ Barthez and Rilliet, p. 249; cited by von Jürgensen.

tions. This form is apt to be unattended by complications and the prognosis is extremely favorable.

Severe and Malignant Measles.—Measles of unusual severity may occur in isolated instances in ordinary epidemics, or the disease may prevail at times in severe form. The factors which determine malignancy are in some instances weakness, debility, and bad hygienic surroundings of the patient, and probably in others an intense virulence of the infection. There are severe cases which are characterized by a normal course of the disease, but exhibit an unusual intensity of all of the symptoms. The fever, catarrhal symptoms, and eruption may all be excessively developed. In the severe and fatal epidemic which we observed a few years ago there was a general tendency to intense confluence of the eruption, so that on the second or third day the rash became quite scarlatinal in appearance.

In some cases characterized by great initial severity the system seems to be overwhelmed by the poison of the disease. The temperature soars to great height (105° to 107° F.), there is profound prostration, great restlessness alternating with stupor, and the patient succumbs before the appearance of the rash. In these *toxæmic* cases the diagnosis may be extremely difficult, and, unless elucidated by the history, quite impossible.

Severity may also be manifested by the early development of *pulmonary complications*. The first few days of the invasive stage may be quite normal, but suddenly the lungs become attacked and a fatal result rapidly ensues.

In the so-called *typhoid* form of measles the disease is ushered in with high fever and great prostration. The skin is hot and dry; there is great thirst and marked muscular relaxation. Nervous symptoms are pronounced, the patient being either apathetic and somnolent or delirious. The tongue is dry and furred, the lips glazed, and the teeth covered with sordes. The abdomen is tender and distended and the bowels often loose. The eruption is poorly developed and bluish in appearance. These cases are usually fatal, death taking place within a week or, less commonly, convalescence may occur after a tedious and protracted illness.

Such cases as the above were not rare during the Civil War. *Camp measles* does not differ essentially from measles seen among civilians save that as a result of privation and exposure the disease is apt to assume a more severe form. Measles is one of the most formidable of camp diseases, as is attested by the morbidity and mortality statistics of the Civil War of 1861. Bartholow says: "In one regiment which came under my observation every man contracted measles who had not had it in early life." The disease was much more prevalent in regiments recruited from country districts. The mortality rate was high. In the general field hospital at Chattanooga it was 22.4 per cent., and in the General Hospital No. 1 at Nashville it was 19.6 per cent.

MALIGNANT HEMORRHAGIC MEASLES.—Black measles was, according to the descriptions of the older writers, much more common years ago

than at the present day. It is also much rarer than hemorrhagic small-pox, with which it has certain features in common. Hemorrhagic measles is more apt to develop in previously ill and debilitated subjects.

The onset of the disease is usually violent, the fever being high and nervous symptoms prominent. The eruption is bluish or purplish in color and fails to disappear upon pressure. In other cases the exanthem may appear, recede rapidly, and be followed by hemorrhagic extravasation into the skin in the form of petechiæ or ecchymoses. At the same time bloody discharges occur from various mucous membranes. There is commonly severe epistaxis and blood may be observed in the urine, stools, and vomited matter. The patient becomes rapidly exhausted, the pulse is frequent and thready, the skin pale and cold, and death closes the scene.

Trousseau describes a fatal case in a girl, aged five years, whom he saw in consultation: "The fever had been constantly accompanied by stupor, which is unusual in this disease. The eruption came out, but the exanthematous patches were of a dark color, that hemorrhagic hue which does not disappear under pressure of the finger. On the eighth day slight delirium supervened, and epistaxis, which had occurred with usual moderation during the first period, became much more profuse. . . . After some hours other hemorrhages developed; she had hæmaturia, bloody stools, and hæmatemesis. Finally, within two days, ecchymotic spots appeared upon the back." The child sank rapidly and died.

It must not be supposed that all hemorrhagic eruptions in measles are necessarily in malignant cases. Attention has already been called to hæmic extravasation into the skin in attacks of average severity.

Irregularity in the Origin and Spread of the Measles Exanthem.—The spread of the eruption of measles involving in succession the face, chest, neck, abdomen, arms, legs, etc., is a tolerably uniform and diagnostic phenomenon. Occasionally a departure from this normal progression takes place. The eruption may, in rare cases, be limited to the face or to the face and trunk. It may begin on the trunk or extremities and involve the face and neck only later. Mayr¹ states that the application of irritants to the skin, such as the use of lotions, ointments, bandages, and compression from other causes may determine the point of origin of the eruption. He is also authority for the statement that in paraplegia from vertebral disease the rash is often absent on the paralyzed lower extremities.

Chairou² reports a curious abnormality of the measles eruption which occurred in a severe epidemic of measles at Rueil in 1862. The eruption lacked intensity, but was accompanied by profuse perspiration and a vesicular eruption similar to the miliary rash seen in lying-in women. Chairou proposed for this condition the name of sweating measles. The constitutional symptoms were severe and uncommon. The course was that of a septic or typhoid measles, with many complications observed

¹ Loc. cit., p. 163.

² Essay awarded a prize by Academy of Medicine of Paris; cited by Trousseau, loc. cit., p. 185.

in typhoid fever, such as periosteal trouble leading to necrosis of the maxillary bones, etc. The mortality rate was high.

Recession of the Rash.—It occasionally happens that the measles exanthem suddenly and prematurely fades after reaching its maximum or even before the height of the eruption is attained. The recession of the rash may be temporary, the eruption later reappearing, or it may be permanent. The lay community has a traditional dread of this “striking in” of the eruption, fearing the involvement of one of the internal organs. As a matter of fact the sudden fading of the exanthem is not the cause, but the result of such condition. The phenomenon is usually due to severe pulmonary involvement, leading to cardiac failure and consequent crippling of the circulatory apparatus. The skin becomes pale and the eruption fades either completely or shows itself as indistinct, bluish spots. With an improvement in the heart action the spots naturally acquire more color and the eruption, so to speak, returns. Thomas believes that rapid disappearance of the eruption does not necessarily indicate the development of some complication. He says: “I have never had an opportunity to convince myself of the connection of a speedy fading of the spots with the sudden occurrence of a complication. A simple rapidly progressing paleness of these can certainly not be considered anomalous.”

Postrubeolic Eruptions.—Reference has already been made to the occurrence of a morbilliform rash, associated at times with renewed fever, developing after convalescence from measles. In rare cases other eruptions may make their appearance about this time. Roger¹ has seen cases, both of recurrent measles and also accidental erythematous rashes after measles. He reports an instance of the latter in a young woman twelve days after an attack of measles, and another in an infant, two and one-half months old, thirty-eight days afterward.

Meyer-Hoffmeister² saw a scarlatiniform erythema during convalescence from measles.

COMPLICATIONS AND SEQUELÆ OF MEASLES.

Larynx.—A moderate grade of catarrhal laryngitis is uniformly present in measles, and is, therefore, scarcely to be regarded as a complication. The laryngeal symptoms develop early in the invasive stage, giving rise to hoarseness, frequent cough, and occasionally spasmodic dyspnoea. The cough is dry, loud and hollow in tone, and in the beginning unproductive of expectoration. The paroxysms of coughing are often violent and incessant, seriously interfering with sleep. Upon the appearance of the cutaneous eruption the cough becomes looser and less frequent and is accompanied by expectoration. Holt states that severe catarrhal laryngitis is present in about 10 per cent. of all cases of measles.

Ulcerative Laryngitis.—Ulcerative laryngitis occurs in a certain proportion of severe cases. In such instances the inflammation is so intense

¹ Loc. cit., p. 875.

² Quoted by Thomas, loc. cit., p. 90.

as to lead to necrosis of the mucous and submucous tissues. The vocal cords are commonly involved in the destructive process. Barthez and Rilliet found ulcerations and erosions in almost one-half of the cases of measles that came to autopsy. Pseudomembranous deposits were present in about one-fifth of the cases.

Gerhardt¹ has seen these ulcerations by laryngoscopic examination during life. He has found them particularly upon the posterior wall of the larynx in cases that exhibit marked stenosis. They may be seen at times early, but are more commonly observed during the eruptive stage. The superficial ulcerations give rise to a rough, dry, frequently repeated cough, accompanied by spasmodic attacks. There is pain upon coughing, speaking, or swallowing, and often considerable dyspnoea.

The most dangerous form of laryngitis is that accompanied by the formation of a pseudomembrane, the so-called *membranous laryngitis*. The fatality of this complication is frightful. In the Hôpital des Enfants Assistés in Paris, Granlou² found this complication 235 times among 1633 cases of measles; out of these 235 patients 218 died, a most appalling mortality.

We have seen a number of these cases that had to be intubated; they all succumbed to the disease. Holt has collected 35 cases of membranous laryngitis out of 2837 cases of measles from miscellaneous sources; he remarks that this complication is more frequent than this in institution epidemics.

Membranous laryngitis may result from the action of the streptococcus, the diphtheria bacillus, and, perhaps, other organisms. Holt states that when the membrane forms in the larynx at the height of the disease it is almost always of streptococcic origin; when it develops at a later period it is usually due to the Klebs-Loeffler organism. The majority of cases appear to be due to pyogenic bacteria. The false membrane is not always limited to the larynx, but may invade the fauces, nose, and mouth. The laryngeal stenosis usually comes on gradually, although more commonly the symptoms may be sudden in their appearance.

The dyspnoea frequently becomes so alarming as to necessitate intubation or tracheotomy. These procedures, however, give, as a rule, but temporary relief, for a fatal bronchopneumonia is almost sure to develop.

The diagnosis between true *laryngeal diphtheria* and membranous laryngitis of streptococcus origin can only be indubitably settled by a bacteriological examination; the former condition is apt to develop late and the latter at the height of the disease. The prognosis appears to be equally desperate in both conditions.

Lungs.—The trachea and larger bronchial tubes are so commonly involved in the catarrhal process in measles that a moderate grade of *tracheitis* and *bronchitis* may be regarded as belonging to the normal symptomatology of the disease. It is only when the inflammatory

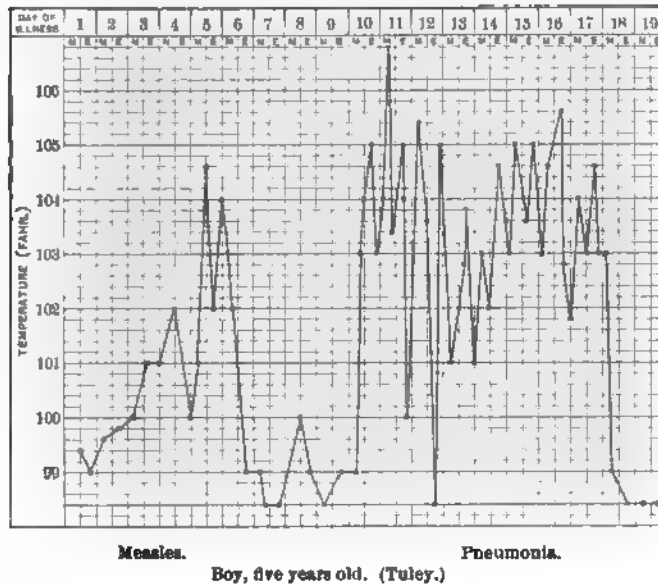
¹ Lehrbuch der Kinderkrankheiten, p. 68.

² La rougeole à l'hôpital des enfants assistés, Paris, 1892.

disturbance is intense and downward extension takes place that the complication assumes a serious aspect. Severe bronchial catarrh usually manifests itself just at or after the height of the eruptive stage; if it be sufficiently widespread, the fever, which at this time falls, will continue to remain elevated. There is frequent coughing, accompanied by mucopurulent expectoration.

Foreign writers still employ the term *capillary bronchitis*; the tendency in this country is to look upon the involvement of the minute bronchioles as an essential part of a bronchopneumonia. The symptoms of capillary bronchitis, therefore, are virtually those of catarrhal pneumonia.

FIG. 81



Measles.

Pneumonia.

Boy, five years old. (Tuley.)

Bronchopneumonia.—Bronchopneumonia is the most common and most fatal of all of the complications of measles. Other conditions fade into insignificance when compared to the slaughter that this complication occasions. Over a half-century ago Gregory wrote: "I am sure I speak much within bounds when I say that nine-tenths of the deaths by measles occur in consequence of pneumonia."

Bartels met with 68 cases of bronchopneumonia among 573 cases of measles, or 11.9 per cent.; Ziemssen and Krabler report 50 attacks of pneumonia among 311 cases of measles, or 16.1 per cent. The figures of Embden give a much smaller incidence—27 attacks in 461 cases, or 5.9 per cent. The frequency of this complication seems to vary considerably in different epidemics. It is much more common in foundling asylums, orphanages, and similar institutions. It is more apt to attack feeble and poorly nourished children and those debilitated by previous illness. This complication is particularly prone to attack children

under two years of age. Holt states that in two epidemics in the Nursery and Child's Hospital, embracing about 300 cases, nearly all in children under three years old, bronchopneumonia occurred in about 40 per cent. of the cases. Of those who had pneumonia, 70 per cent. died. Henoch says that a certain amount of pneumonia is seen in nearly all fatal cases of measles.

Bronchopneumonia usually manifests itself when the eruption begins to decline, although the onset may be delayed to a later period. The post-eruptive decline in the temperature fails to occur, the fever instead remaining in the neighborhood of 103° F., with, perhaps, morning remissions of a degree or so. The pulse is greatly increased in frequency, and the respiration is shallow and hurried, and not infrequently labored and difficult; it is a pitiful sight to see the little patient with dilating nostrils and a livid countenance raise itself in the bed to relieve its distressed breathing. The cough may be short and repeated or infrequent and spasmodic. In unfavorable cases there is protracted fever, progressive increase in the rapidity of respiration (60 to 80), cold extremities, extreme weakness, and rapid-running pulse. Nourishment is refused and, when taken, is often vomited. Great pallor develops and toward the end a characteristic lividity is seen. A few hours before death the temperature may rise to great height, 107° or 108° F. In favorable cases the temperature at the end of ten days or two weeks declines gradually to normal, the cough lessens, the respiration improves, the child becomes brighter, desires more food, and takes an increasing interest in its surroundings.

The symptoms that indicate the presence of a bronchopneumonia are protracted fever, cough, rapid pulse, hurried and labored breathing, and prostration. Percussion will often discover some dulness over one or both of the lower lobes posteriorly; the respiratory murmur is diminished and bronchovesicular breathing is heard; in addition to the coarse rales heard in the larger tubes, fine, moist rales are audible over the small, consolidated areas.

Lobar Pneumonia.—Lobar or croupous pneumonia is a much less frequent complication of measles than the catarrhal form, and is apt, when it occurs, to develop in older patients. This form of pneumonia is characterized by higher fever with fewer remissions, by its limitation to one lung or lobe thereof, by the presence of pleuritic pains, a shorter course terminated by crisis, and a lower mortality rate.

Pleurisy.—Pleurisy with effusion is an unusual complication of measles. In some epidemics it may develop secondarily to a severe pneumonia, in which case it is apt to eventuate in an empyema.

Fürbringer¹ calls attention to the occasional occurrence of a primary pleurisy with effusion. He has observed a number of cases, most of which ran an acute course and were probably purulent from the beginning.

Pulmonary Tuberculosis.—Pulmonary tuberculosis may manifest itself as a termination of a long-standing bronchopneumonia occurring after

¹ *Eulenberg's Real-Encyclopaedia*, vol. xii., second edition, p. 559; quoted by von Jürgensen.

measles. The bronchial catarrh and the lowered resistance of the patient render the implantation of tuberculosis readily explicable. In cases in which a latent glandular tuberculosis, particularly of the thoracic lymph nodes, has existed, the attack of measles stimulates the previous disease to noxious activity. In some cases tuberculosis may develop as a direct sequel of measles, an irregular temperature persisting after the incomplete convalescence from the latter disease. The tuberculous disease may take the form of an acute miliary tuberculosis. Holt truly says: "An attack of measles in a child with tuberculous antecedents should always be looked upon with apprehension."

Barthez and Rilliet have observed *gangrene of the lungs* in four instances, and Steiner and Neureutter have met with this complication in two patients. This much to be dreaded condition may have its origin in a severe bronchopneumonia.

Alimentary Tract.—From what has already been said concerning the measles exanthem it is evident that a mild inflammation of the buccal and pharyngeal mucous membrane is uniformly observed. This comes on in the invasive stage and tends to subside as the cutaneous eruption increases in development.

The cheeks, gums, tongue, soft palate, tonsils, and pharyngeal wall all participate in the catarrhal process. In feeble and debilitated children this inflammation, especially under the influence of infection with pyogenic and other bacteria, may lead to complications which are not only subjectively distressing, but of serious import. *Aphthous stomatitis* has been reported by a number of writers. The sores may give rise to much pain and interfere with the desire of the child to take nourishment. *Ulcerative stomatitis* not infrequently develops, particularly in the buccogingival furrow. This is characterized by the formation of small patches covered with grayish, necrotic epithelium. When the dead epithelial covering is cast off there are disclosed to view ulcerations of varying depth, with sharp and irregular edges; the base is frequently covered with a pseudomembranous deposit. These losses of tissue are not infrequently seen on the gums, and about the lips, particularly the oral commissures; in the latter regions each movement of the mouth causes pain and induces bleeding. In poorly nourished children these ulcerations may last for a long time before complete healing occurs.

A fortunately rare but most frightful complication of measles is that form of gangrene variously designated *cancrum oris*, *gangrenous stomatitis*, or *noma*. The fatal character of this complication makes the condition of sufficient importance to warrant a description elsewhere. To be sure, there are less serious forms of gangrenous stomatitis in which the loss of tissue is circumscribed. We have not infrequently seen necrosis of a portion of the gum and subjacent alveolar process which, after the throwing off of the slough, has been followed by thorough healing; in some of these cases a portion of the bone and the neighboring teeth have come away.

In a certain proportion of cases *membranous patches* may be seen

on the tonsils and neighboring palatal mucous membrane. This process may spread downward into the larynx and give rise to the dreaded membranous laryngitis. The pseudomembrane may be of streptococcic or staphylococcic origin like the exudate seen in scarlatina, or it may be true diphtheria. In some cases *tonsillitis* is observed, in which event there is enlargement and congestion of these structures and pain upon swallowing.

The stomach is but rarely the seat of any serious complication.

Diarrhœa.—Diarrhœa is a common and not infrequently a serious accompaniment of measles. It may exist in all grades, from a slight catarrhal enteritis, lasting but a few days, to a severe enterocolitis with fatal outcome. As would naturally be expected, diarrhœa is more common in the summer months and especially in extremely hot summers. This complication is also more frequently observed in tropical and subtropical countries. Gregory says: "In India and other hot countries thoracic complications are rare; diarrhœa and dysentery prove the usual and most troublesome sequelæ." It is not at all uncommon for a mild diarrhœa to be present in the invasive and early eruptive stages. There are frequent loose and watery movements, with or without pain, which tend to subside as the eruptive stage advances. The severe forms of enteritis and ileocolitis usually develop late during the decline of the eruption. In some cases the large intestine is involved and symptoms of dysentery manifest themselves; pain and tenesmus are present and frequent; small, bloody stools containing mucus are passed.

Diarrhœa appears to be more common in some epidemics than in others. Willischanin¹ observed an epidemic of measles in a girls' school in which 10 out of 50 of the patients had diarrhœa during convalescence. It lasted from three to five days and was believed to be due to the elimination of special toxins.

Intestinal inflammation is most frequently observed in infants and young children, in whom it not infrequently leads to a fatal termination. Cases are on record, however, in which adults have succumbed to measles as a result of this complication.

Nervous System.—As is the case with most infectious diseases, measles may be accompanied or followed by a great variety of disturbances due to involvement of the brain, spinal cord, or the peripheral nerves. When the fact is recognized that measles attacks almost the entire human family, the relative infrequency of nervous complications may be appreciated.

Mental Disorder.—Measles is, in rare instances, followed by insanity, which usually takes either the form of mania or dementia. Christian² reports a case of temporary mania and paralysis. Finkelstein³ saw 2 cases of mania after measles, and Bond⁴ observed a case developing on the eighth day of the disease. Weber noted delusions of persecution in one of his patients. In an epidemic of 108 cases occurring in an insti-

¹ St. Petersburg med. Wochen., December 4, 1893; quoted by Williams, loc. cit.

² Centralbl., 1874, p. 95.

³ Maryland Medical Journal, January 29, 1896.

⁴ Vratsch, 1886, No. 20.

tution in Virginia and reported by Smith and Dabney, insanity ending in recovery developed in three patients.

Beach¹ analyzed 2000 cases of idiocy and found 37 (1.85 per cent.) which could be traced to attacks of infectious diseases; of this number 11 were attributed to attacks of measles. Nearly all the cases, however, were in persons with neurotic antecedents.

Cerebral and Spinal Paralysis.—Paralysis following measles is a rare complication. Allyn² was able to collect but 41 instances, 35 of which were palsies of cerebral origin. The onset of the complication is abrupt, and commonly, though not always, marked by convulsions. In other cases somnolence or coma occurs in the beginning. Following upon the convulsions or coma the evidences of paralysis are observed. In spinal paralysis coma and convulsions are absent. The paralyzes, according to Allyn, usually appear during convalescence and most frequently from the latter part of the first to the close of the third week after the onset of the attack. Of 21 reported cases, 11 developed palsy between the fifth and sixteenth day, while 5 more probably belong to this period, although the data are imperfect. In the remaining cases 3 developed convulsions on the second day of the eruption, 1 a month after the onset of the measles, and 1 in from five to six weeks. The prognosis as to life is good. In only 4 of the cases did a fatal result ensue. In some of the cases the lesions were more or less permanent, aphasia and muscular atrophy persisting some years after the attack. The paralyzes collated by Allyn were chiefly cerebral palsies of the hemiplegic type, but included also disseminated myelitis and ascending spinal palsy.

Cases of paralysis have since been reported by a number of authors. Dawson Williams³ saw a case of disseminated sclerosis in a girl three and a half years old on the fourth day of an attack of measles.

Bruce records a case of diffuse myelitis and Barlow an extensive softening of the cord. Ormerod observed paralytic symptoms one month after measles in three children. Andeoud and Jaccard⁴ report a case of vesical paralysis in a nine-year-old girl, and Ortholon⁵ a true paraplegia in a three-year-old girl.

Paralysis after measles has also been reported by Graf,⁶ Morton,⁷ and Ellison,⁸ who observed a case of acute ascending myelitis.

False Disseminated Sclerosis.—There occasionally occurs in measles, as in smallpox and other infectious diseases, sudden unconsciousness followed by loss of power of speech and certain other paretic and ataxic symptoms. This may occur during the febrile stage or during convalescence. Rapid recovery may ensue or a train of symptoms may develop suggesting disseminated sclerosis. Instead of the condition being progressive there is a distinct tendency to improve.

¹ British Medical Journal, 1895, vol. ii. p. 707.

² Med.-Chir. Soc., November 28, 1893.

³ Thèse de Bordeaux, November 28, 1894.

⁴ Indiana Medical Journal, 1892 and 1893, p. 176.

⁵ Archives of Pediatrics, 1897, vol. xiv. pp. 541-544.

⁶ Medical News, November 28, 1891.

⁷ Rev. méd. de la suisse romande, 1894.

⁸ Lancet, 1896, vol. ii. p. 1077.

Barthez and Sanné have collected a series of 8 cases characterized by paresis of the soft palate, pharynx, tongue, and muscles of the neck. In 4 cases the symptoms appeared early in the course of measles, and in the remaining 4 at the end of three weeks. Recovery took place in all of the cases in from three to twenty days.

Meningitis.—Instances of inflammation of the membranes of the brain have been reported by Spiess, Voit, Meyer-Hoffmeister, Kellner, Constant, Löschner, Thore, Bufalini, King, Mettenheimer, and Harvey.¹ Frank, Rilliet, and Starck have observed spinal meningitis after measles.

Chorea.—Chorea is an occasional sequel of measles. Cases have been recorded by Sibergundi, Böning, and others. In an analysis of 439 cases of chorea made by Stephen MacKenzie for the Collective Investigation Committee of the British Medical Association, measles or measles and anæmia were found to be the sole antecedent illnesses in 49 cases—nearly 9 per cent. Barthez and Rilliet have noted after measles a prompt recovery from a chorea of some months' duration.

Skin.—Mention has already been made of the accidental erythematous rashes which may, in rare cases, precede or follow the true exanthem of measles.

During the invasive period it is not rare for *herpes facialis* to appear, a phenomenon which develops in many infectious processes. *Urticaria* may also occur either in the course of the disease or at a later period. The urticarial eruption is usually moderate and of short duration. Claus² reports urticaria occurring in two cases of measles during the period of incubation.

Several authors have called attention to the development of a *bullous eruption* resembling pemphigus. Cases have been reported by Krieg,³ Löschner, Henoch,⁴ Steiner,⁵ Du Castel,⁶ and recently by Baginsky.⁷ Steiner saw 4 cases, all in the same family. The blebs varied in size from a pea to a pigeon's egg, came out in crops, attacked both the skin and mucous membranes, were accompanied by fever, and occurred at any time during the course of the disease, before, during, or after the measles exanthem.

In Henoch's⁸ patient the bullæ were so large that a single one covered each cheek; 2 out of these 5 cases terminated fatally. Masarei⁹ saw upon the palms and soles during desquamation large blebs which burst and left obstinate and painful ulcers.

Gangrene may attack other parts of the skin than the cheek and genitalia, which are the most common sites of the process. Thomas, of Paris, has reported an extensive gangrene of the buttocks in a child

¹ Journal of the American Medical Association, 1897, vol. xxix. pp. 1149-1151. The other authors mentioned are quoted by Thomas.

² Jahrbuch f. Kinderh. u. Phys. Erzieh., June, 1894.

³ Cat. Jahrbuch, 1843, p. 219.

⁴ Berlin. klin. Wochenschrift, 1882, p. 193.

⁵ Jahrbuch f. Kinderh., new series, vol. vii. p. 346.

⁶ Rev. gén. de clin. et de therap., Paris, 1897, vol. xi. p. 609.

⁷ Archiv f. Kinderh., 1900, Bd. xxviii., H. 1 and 11.

⁸ Mentioned by von Jurgensen, loc. cit., p. 300.

⁹ Quoted by Thomas.

two years of age. Mayr, Faye, Battersey, and Carroll¹ report instances of gangrene attacking various portions of the cutaneous surface.

Impetigo, boils, and abscesses are occasionally observed during convalescence from measles. They represent varying grades of infection with the common pyogenic organisms. *Eczema* occasionally makes its initial appearance after an attack of measles and may persist for an indefinite period. On the other hand, chronic eczemas have been known to disappear after an attack, as in cases reported by Behrend and others. *Psoriasis* has been observed to appear for the first time after measles. Measles, of course, does not cause the psoriasis, but merely determines the date of its outbreak.

Disseminated tuberculosis of the skin may follow in the wake of measles, as in the cases reported by Du Castel,² Haushalter,³ and Adamson.⁴

Du Castel saw 3 cases and remarks that "it is not exceptional to see a disseminated tuberculosis of the skin as a sequel to measles." This usually attacks the face, legs, and especially the upper extremities. The lesions appear soon after the decline of the measles eruption in the form of small, deep-red nodules. Haushalter saw 2 cases of scrofulous lichen, 1 of which later developed enlarged glands and tuberculous gummata. Adamson's case was one of multiple warty lupus occurring on the arms and legs. The patient subsequently developed a post-pharyngeal abscess and later hip disease.

Roger⁵ observed, in the spring of 1900, 4 cases of *erythema nodosum* after attacks of measles. A girl, aged seventeen years, eleven days after the termination of an attack of measles of moderate intensity, developed fever, and twenty-four hours later a typical erythema nodosum of the legs and subsequently the arms, accompanied by painful joints; the condition lasted fifteen days.

The other 3 cases were analogous; they occurred in patients fifteen, seventeen, and twenty-six years of age, respectively. Fever appeared from nine to ten days after the termination of measles. The erythematous nodes and the joint involvement persisted from seven to ten days.

Eyes.—Ocular complications are not rare in measles, a fact which is easily explained by the severe catarrhal involvement of the conjunctiva during the invasive and eruptive stages. The eyes are particularly apt to suffer in scrofulous children. Corneal ulcerations may occur, and, in bad cases, lead to perforation and general panophthalmitis. It is not rare for obstinate blepharitis, granular lids, or keratitis to persist a long time after convalescence from the original disease. Comby states that proper care of the eyes greatly reduces the number of ocular complications, and in support thereof mentions the fact that he observed only 17 cases of conjunctivitis of moderate intensity among 715 cases of measles.

¹ Quoted by Thomas.

² *Annal. de derm., etc.*, 1898, tome ix., Nos. 8 and 9, p. 729.

³ *Ibid.*, No. 5, p. 455.

⁴ *British Journal of Dermatology*, 1899, p. 20.

⁵ *Loc. cit.* p. 875.

Ears.—Inflammation of the middle ear is by no means an uncommon complication of measles, although it does not develop as frequently as in scarlatina. The catarrhal inflammation of the nasal passages frequently extends along the Eustachian tubes to the middle ear. Bezold¹ carefully explored the ears in 16 fatal cases of measles, in all of which he found inflammatory changes. The tympanic cavity contained either a mucopurulent exudation or a material that was frankly puriform. The streptococcus pyogenes was present in about 50 per cent. of the cases; in the other half the staphylococcus aureus and albus were found. The mucous membrane is red, swollen, and covered with a mucopurulent or seropurulent exudate. Tobietz² examined the ears of 22 cases of measles at autopsy and confirmed the above-mentioned findings.

Both of these writers are in accord as to the early development of the aural catarrh. The ear trouble is not regarded as due to a secondary infection, but is rather the result of the localization in this region of the enanthem. Catarrhal otitis may therefore develop in the early eruptive period. In a case studied by Tobietz that died twenty-four hours after the appearance of the eruption, otitis was already present.

This early otitis is comparatively mild and usually does not lead to perforation of the tympanic membrane. The later-developing otitis media usually results from infection from the nasopharynx, and is much more prone to end in suppuration and perforation.

Severe purulent otitis media appears to be more common in some epidemics of measles than in others. Downie³ states that children who have adenoid vegetations and suffer from catarrh of the throat and nose are more apt to develop middle-ear trouble. He furthermore claims that the horizontal posture of the sick child favors Eustachian infection and retention of the inflammatory products within the middle ear. Of 501 cases of tympanic involvement in children seen by Downie, the condition was attributable to measles in 131 instances, or 26.1 per cent. Curiously, only 63 cases (12.6 per cent.) were observed that developed during an attack of scarlet fever.

It is not always easy to diagnose the onset of an otitis media, particularly in young children who are unable to make verbal complaint. The complication most commonly develops about the end of the second week. Children are cross and fretful, frequently toss the head and cry out with pain. The temperature is usually elevated and may rise to great height. When an otherwise inexplicable rise of temperature occurs about this time, the possibility of purulent otitis must be considered. Inspection of the tympanic membrane is not an easy task in young children. When this can be accomplished the membrane is seen to be congested and lustreless, and when pus is present the tympanum bulges into the meatus, the puriform secretion shining through the lower tympanic segment.

In severe cases of middle-ear disease necrosis of the ossicles or of the

¹ *Münchener med. Wochenschrift*, March, 1896.

² *British Medical Journal*, 1894, vol. ii. p. 1163.

³ Quoted by Comby, *loc. cit.*

surrounding bony walls may take place. Burkner¹ says: "An invasion of the labyrinth by cocci causing necrosis has been repeatedly demonstrated of late. The lesion results in a very serious loss of functional power." The suppurative inflammation may extend to the mastoid cells or, in rare cases, to the membranes of the brain. Ashby and Wright have pointed out the fact that infection may take place through the petromastoid suture, which in infancy is still ununited. Purulent meningitis, abscess of the brain, or thrombosis of the lateral sinus might thus develop. In general it may be stated that middle-ear trouble complicating measles is less serious than that which occurs in scarlet fever.

Many cases of *deaf-mutism* are traceable to attacks of measles. Kerr, Love, and Addison² have collected statistics from institutions in Great Britain which show that of 1140 deaf-mutes, 138, or 9.8 per cent., attributed their loss of hearing to attacks of measles. Of 1673 acquired cases in American institutions, 52, or 3.1 per cent., were due to measles. Among 1989 acquired cases on the continent of Europe, 84 cases, or 4.2 per cent., were ascribed to this disease.

In these cases the deafness results from destructive changes in the internal ear which have resulted from extension of the inflammatory process from the middle ear.

The Heart.—Endocarditis, pericarditis, and myocarditis are rare complications of measles. Inflammation and degeneration of the cardiac muscle may occur in malignant cases, particularly when there is hyperpyrexia. We recall a malignant family epidemic some years ago which destroyed the lives of the three children of the household. The first child sat up in bed during convalescence and dropped back dead. The other two succumbed to a profound toxæmia.

Cases of *endocarditis* have been reported by Martineau, West, and Köbler. Hutchinson³ records 4 cases in which mitral murmurs developed during the course of measles, and Cheadle refers to 2 cases found in the post-mortem records of Great Ormond Street Hospital. Comby discovered mitral insufficiency in a girl nine years old, after an attack of measles. Although Sansom⁴ states that the influence of measles in predisposing to endocarditis has been much underrated, most writers are of the opinion that this complication is a rarity.

Pericarditis, according to Autenrieth, is not infrequent. Cases have been reported by Berndt, Majer, Espinouse, Braun, Siegel, Mettenheimer, and Heyfelder.⁵ When pericarditis occurs it is apt to be associated with a pleuropneumonia.

Kidneys.—Renal complications are rare in measles, their infrequency contrasting sharply with their prominence in scarlatina. Nevertheless, Baginsky says that his recent experience leads him to believe that they would be discovered more often if carefully looked for.

¹ *Behandlung der bei Infektionskrankheiten Vorkommenden Ohraffectionen*, loc. cit., p. 581.

² *Deaf-mutism, a Clinical and Pathological Study*, Glasgow, 1896; cited by Dawson Williams, loc. cit.

³ *Med.-Chir. Trans.*, 1891, vol. xxiv.

⁴ Quoted by Williams, loc. cit.

⁵ Mentioned by Thomas, loc. cit.

Febrile albuminuria of brief duration is not uncommon in well-pronounced attacks of measles, as in other infectious processes accompanied by fever. When the kidneys are seriously involved there may be general anasarca, as in cases reported by Abeille, Denizet, and Comby (2 cases). Ascites and anasarca may, however, occur without albuminuria, at times in association with chronic diarrhoea.

Cases of true nephritis have been placed on record by Geissler, Röser, Frank, Rilliet, West, Kjellberg, Lehman, Bouchut, Malmsten, Spiess, Hauner, Steiner, Neuretter, Zehnder, and Thomas, who cites these various writers. Fatal cases with uræmic symptoms have been reported by Müller, Demme, Browning, and Zichy-Woinarski.¹

Vulvitis.—Among 715 cases of measles treated in isolation pavilions, Comby observed vulvitis twenty-five times, an incidence which he thinks was kept relatively infrequent through systematic antiseptic irrigations. The inflammation of the vaginal orifice and vulva begins early, as a rule, and may persist for some time. The parts are red, swollen, covered with a mucopurulent discharge, and extremely tender. Micturition is accomplished with considerable pain. In some cases vulvar ulceration occurs and more rarely gangrene.

Glands.—A moderate grade of adenopathy is a part of the normal symptomatology of measles. In some cases the lymphatic glands become greatly enlarged, particularly in the cervical region. In rare cases suppuration may take place, as in cases mentioned by Gregory and Rilliet.

In other cases the glandular enlargement may persist for a long time and eventually terminate in glandular tuberculosis. This is particularly true of the bronchial glands. Fichtbauer, Thore, Eiseman, Bufalini, and Battersey² have reported cases of inflammation of the parotid gland accompanying measles, and Seidl, Schultze, and Kellner have seen the parotids involved at a later period.

Purpura.—Hemorrhages developing late in the course of the disease or during convalescence should not be interpreted as evidence of malignant hemorrhagic measles, but as a secondary and superadded condition. Nearly all of the exanthemata may at times be complicated at a late stage by the development of hemorrhages into the skin and from the various mucous membranes, including the kidneys and intestines.

Masarei³ saw eight patients convalescing from measles attacked with fever, dropsy without albuminuria, and "scurvy, mostly in the form of purpura;" all of the cases ended fatally. Gley⁴ saw intense purpura hemorrhagica, together with scorbutic appearances in the mouth, some days after the disappearance of the measles rash.

Gangrene.—Although gangrene is not a common complication of measles, it appears to occur more often after this infection than any other, excepting, of course, cutaneous gangrene in smallpox.

The necrosis is apt to take the form variously designated as *cancrem oris*, *gangrenous stomatitis*, or *noma*. This formidable complication

¹ Australian Medical Gazette, October 15, 1893.

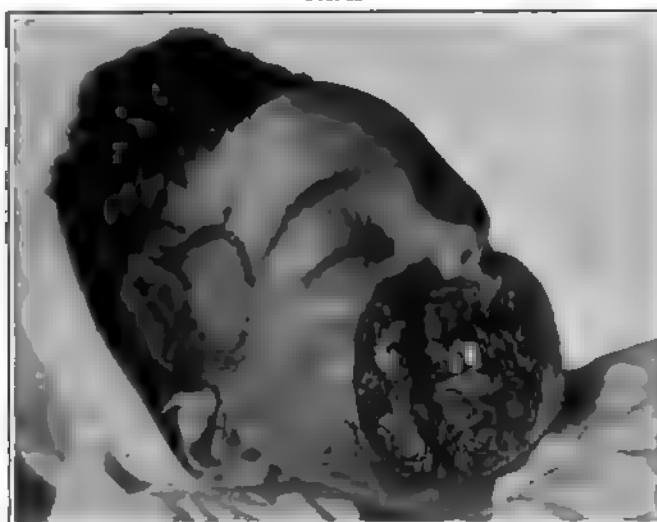
² Quoted by Thomas.

³ Quoted by Thomas, p. 104.

⁴ Quoted by Thomas.

commonly develops during the decline of the eruption. It is often associated with or preceded by an ulcerative stomatitis. The symptoms that first attract attention are salivation and a fetid breath. If the mouth is inspected there will usually be found, between the commissure of the mouth on the affected side and the opening of Steno's duct, a vesicular elevation of a violaceous color; this becomes gradually darker and finally gives way to a blackish, pultaceous mass. The corresponding portion of the cheek on the exterior is swollen and of a wax-like pallor. Soon a bluish-red spot appears, which becomes gangrenous and breaks through. From this point the necrosis now spreads in all directions. The spreading border is surrounded by a dusky-red zone which is firm and infiltrated. The immediate spreading edge shows a raising up of the epidermis in the form of a vesicular ring. There may be an extension

FIG. 82



Fatal cancerum oris after measles. The necrotic tissue has been removed, exposing to view the alveolus and teeth.

of gangrene from one-quarter of an inch to an inch in twenty-four hours. The gangrenous process in severe cases involves the entire cheek and the greater part of the nose and lips. It has been known to attack the ear, the eyelids, and a considerable portion of the neck. Usually the patient dies of exhaustion before such ravages are possible. In a small proportion of cases the gangrene ceases, a line of demarcation is formed, and the sphacelated tissues are gradually thrown off. In such instances the deformity must subsequently be remedied by a plastic operation. In the fatal cases there is great prostration, the child takes nourishment with difficulty, and death takes place ordinarily in from one to two weeks. A horrible odor emanates from the patient, which pervades the entire room in which he lies.

There is a less serious form of gangrenous stomatitis in which the

Fig. 83



Gangrenous oris complicating measles. Photograph taken two days after the cutaneous lesions became involved.

Fig. 84



Same patient as Fig. 83, showing the spread of the gangrene. Photograph taken three days after the previous picture.

necrotic process is limited to the mucous membrane and bony tissues of the mouth. This commonly has its origin about the gums and alveolar process. After the loss of some of the teeth and a portion of necrosed alveolus, the process may cease and recovery take place. In some cases, however, this bony necrosis is merely part of the general gangrenous process which attacks the cheeks.

The necrotic process may, in rare cases, attack the genitalia, particularly of female children, giving rise to the condition known as *noma pudendi*. The course of the gangrene does not differ from that involving the mouth.

FIG. 85



Same patient as Figs. 83 and 84. Photograph taken after death on the eighth day after the beginning of the gangrene, and three days after Fig. 84.

Measles has preceded about one-half of the cases of *cancrum oris* on record. In 106 cases of gangrene of the mouth, Tourde found 41 to follow or accompany attacks of measles. Caillout and Bouley, in 46 cases of gangrene of the mouth, noted measles as an antecedent disease in 40 instances. Mahieux saw measles produce gangrene of the mouth in 3 out of 11 cases. Thus, in 163 cases of gangrene of the mouth measles preceded in 84, or over 50 per cent.¹

Rilliet and Barthez observed 11 children with measles attacked with gangrene; the localization was as follows: gangrene of the mouth, 8 times; gangrene of the lungs, 4 times; gangrene of the pharynx, 3 times; gangrene of the larynx, once. The gangrene appeared in several localities in some of the patients. Moynier saw 6 cases of gangrene in

¹ Mentioned by Moynier. Des accidents graves de la rougeole, etc., Metz, 1860.

measles. In 4 cases the vulva was attacked, 2 dying. Gangrene was noted five times attacking the skin, the following regions being selected. abdomen, face (twice), arm, and buttock. A number of other cases of gangrene of the mouth were observed. Pneumonia and diarrhoea were frequent complicating conditions.

Hildebrandt¹ and Pertbes² from the literature have collected 133 cases of cancrum oris in which the antecedent or accompanying disease is mentioned. Noma accompanied or followed measles in 53 cases. The diseases are as follows:³ measles, 53 times; typhoid fever, 26 times; chronic diarrhoea, 21 times; scrofula, 19 times; smallpox, 9 times; diphtheria and measles, twice; diphtheria and typhoid, once; diphtheria of the genitalia, once; diphtheria and scarlet fever, once.

The affection is extremely rare in infancy and beyond the age of puberty; it may be remarked that measles is also uncommon during these periods. Von Bruns⁴ collected 413 cases of noma, among which only 6 cases occurred in infancy.

The cause of noma is but poorly understood. It has been variously attributed to embolism, nerve involvement, the use of mercury, and infection with some necrotizing micro-organism. The last-named theory is doubtless correct, although the identity of this microbe does not appear to have been determined.

Walsh⁵ made a careful bacteriological study of 8 cases of noma occurring in a home for children in Philadelphia. It is an interesting fact that these cases occurred during a period of two and one-half years. The diphtheria bacillus was recovered by culture from each case. Inoculation and tinctorial tests were employed to identify the Klebs-Loeffler organism. Most of the cases followed measles, but several occurred after diphtheria. Four of the cases began with ulcerative stomatitis. A number of the cases of ulcerative stomatitis—15 in all—were cultured, but diphtheria organisms were not found. Walsh states that "since noma is a species of moist gangrene, requiring probably from analogy two different micro-organisms, one a saprophyte to produce putrefaction, another a parasite to produce primary necrosis, it is possible that in these cases where diphtheria bacilli are found they may be the primary causative agents. When other pathogenic micro-organisms capable of producing necroses are found, it is possible that they may be the primary excitants."

The above investigation is of considerable interest, particularly in view of the painstaking manner in which it was carried out. The result, however, is scarcely in harmony with our clinical experience. We have observed 4 cases of fatal cancrum oris within recent years; 3 occurred with measles following scarlet fever, the other with measles alone. We have never had a case of noma develop in the diphtheria wards, although on a number of occasions measles has broken out there.

¹ Dissertation, Berlin, 1873.

² Verhandl. deutsch. Gesellsch. f. Chir., 28 Kongress.

³ Mentioned by Walsh, Diphtheria Bacilli in Noma. Proceedings of the Philadelphia Pathological Society, June, 1901.

⁴ Handbuch der prakt. Chir., Band I., Abth. 2.

⁵ Loc. cit.

Noma is regarded by Matzenauer¹ as a form of hospital gangrene, but feebly contagious and requiring, as a rule, a severe preceding disease to produce a predisposition. He discredits the diphtheria bacillus as an etiological factor, and believes the exciting organism is the same anaërobic rod-shaped bacillus that is found in hospital gangrene.

One fact is undoubted, that measles for some reason more strongly predisposes to the development of noma than any other affection. Babes and Zambilovici² announce that they have discovered a very small bacillus, cultures of which injected into the cheek of a rabbit have given rise to gangrene similar to noma.

The mortality of noma is frightful, about 70 per cent. of the patients succumbing to the disease.

Pregnancy.—Measles in *pregnant women* is uncommon, inasmuch as most individuals pass through an attack of measles in childhood. As is true of nearly all infectious diseases, the development of measles in parturient women is apt to prematurely terminate the pregnancy. Rösch has reported a case of abortion terminating fatally as a result of measles.

Incidental Improvement in Chronic Diseases After Measles.—Every infectious disease produces a certain systemic commotion or change; this may favor the development of diseases to which the patient may be inclined. On the other hand, existing diseases, sometimes of long duration, may disappear after such a systemic shaking-up. Thomas has collected a number of interesting instances from which we freely quote.

Behrend saw an eczema of the scalp of three years' duration, in a woman of forty years of age, permanently cured after an attack of measles. The curative influence of measles upon long-standing diseases of the skin has also been attested by Rilliet, Taupin, Guersent, and Rayer. Barthez and Rilliet saw chorea, epilepsy, and incontinence of urine of several months' duration get well after measles.

According to Weisse, a girl who suffered from convulsions was entirely cured. Guersent noticed, with the beginning of the fever of measles, permanent relief from epileptiform seizures, of which the patient had had several a day for a long time. Schmidt saw a six-year-old girl, who had had daily convulsions that had so reduced her strength that death was expected, completely recover after measles. Feith and Schröder van der Kolk report the case of a woman who for five years was confined to an asylum because of violent attacks of mania, who, after measles, was cured and discharged from the institution. Hildebrandt saw an obstinate disease of the joints, which had been unsuccessfully treated for three years, promptly get well after convalescence from measles. Schmidt noted an almost magical recovery in a five-year-old boy with contraction of the lower extremities of six months' duration. Of course, such examples of the accidental curative influence of an attack of an infectious disease are met with not only

¹ Arch. f. Derm. u. Syph., 1902, No. 60, p. 373.

² Quoted by Roger, loc. cit., p. 402.

after measles, but also at times after other processes. Mention is made elsewhere of a raving maniac, confined in an insane asylum, who was completely cured after an attack of smallpox.

Coincidence of Measles with Other Infections. Measles may be complicated by almost any of the known infectious diseases. In the association of several infectious processes measles may be the primary disease, or it may develop secondarily after some other infection. We have, on a number of occasions, seen measles complicate diphtheria and scarlet fever. We are inclined to believe that the prognosis is more serious when measles is the secondary infection than when some other disease is engrafted upon it. We have seen measles develop during convalescence from smallpox and have also observed the reverse order.

In the vast majority of cases the one disease develops during the decline of the other. We have never seen measles in its early eruptive

FIG. 66



Boy exhibiting eruption of measles which developed during convalescence from smallpox.

stage complicated by a second infectious disease. Measles and whooping-cough seem to succeed each with more frequency than any other disease. Among 166 cases of measles, Bernardy¹ saw pertussis develop in 21 instances.

THE PATHOLOGY OF MEASLES.

Skin. At autopsy the eruption of measles is not visible unless there has been hæmic extravasation into the skin.

The skin has been studied histologically by Neumann, Catrin, and Unna. Neumann² found as the chief changes a round-cell infiltration about the bloodvessels, hair follicles, and sweat glands. Catrin³ likewise observed a pronounced infiltration of leukocytes, but in addition, in the nodular form of measles, a series of changes in the deep epidermal cells.

¹ *Annals of Gynecology and Pediatrics*, July, 1894.

² *Histolog. Veränderungen der Haut bei Masern*, u. Scharlach. *Med. Jahrb.*, 1882, p. 159.

³ *Les altérations de la peau dans la rougeole*. *Archiv de méd. exper.*, 1891, No. 2, quoted by Unna.

These consisted of a colloid degeneration of the perinuclear zone of some of the deep-lying epithelial cells. Around the areas of colloid change were dilated interepithelial spaces containing coagulated fibrin and leukocytes. In the centre of the papule the colloid masses run together and undergo coagulation necrosis, this taking place in the prickle layer.

Catrin only found emigration of leukocytes from the papillary blood-vessels at those places where the surface epithelium contained colloid cells. Unna regards the colloid change and necrosis of the epithelium as the result of the direct influence of the poison of the disease upon the epidermal structures.

Unna¹ states that in measles a spastic resistance in the cutaneous vessels is added to the primary congestive hyperæmia which develops around the infection in the capillaries, and this explains the cyanotic color, the papular swelling, and the urticarial œdema of the centre, as well as the frequent escape of coloring matter of the blood. The rapidly developing spastic œdema always collects at the place of least resistance, which, in children, is in the fatty tissue around the coil glands and in the sheaths of the larger vessels, the cutaneous muscles and follicles. The individual coils, the hair follicles, and the muscles seem to swim free in widely dilated spaces.

Dilated lymph vessels and enormously distended lymph spaces are seen in the lower and central parts of the cutis. Another characteristic is the almost complete absence of a cellular exudate. Leukocytic emigration is not more than in all simple stagnatory hyperæmias, less, indeed, than in most. But a few leukocytes are found in the epithelium. During the stage of scaling, the subbasal horny layer separates itself from the basal and, with the central and upper horny layers, form the scale. The lost epithelium is replaced, as usual, by mitotic proliferation. The above description, Unna remarks, refers merely to the ordinary flat or slightly papular eruption.

Mucous Membranes.—The mucous membrane of the nose, mouth, pharynx, larynx, trachea, and bronchi is the seat of a catarrhal inflammation. The epithelial cells undergo a colloid change and are often swollen and detached. The lymph follicles and the surrounding structures are infiltrated with cells. Occasionally when the inflammation is intense the follicles may break down and form ulcers. At times such ulceration in the larynx may lead to involvement of the cartilage. Slawyk,² in a histological study of the oral mucous membrane, found the epithelium thickened and in places undergoing fatty degeneration, giving rise to the whitish dots described by Koplik.

Steiner³ observed in several cases, at autopsy, a blotchy redness of the mucous membrane of the larynx and bronchi, and Wilson, Eisenmann, Rayer, and Gerhardt saw a similar condition in the trachea and bronchi.

Heyfelder,⁴ one of the older writers, describes an eruption similar to that on the skin in the duodenum, jejunum, and, at times, in the stomach

¹ *Histopathology of the Skin*, translated by Dr. Norman Walker, 1900.

² *Deutsch. med. Wochenschrift*, April 28, 1898; quoted by Corlett.

³ Quoted by Thomas, *loc. cit.*, American edition, p. 72.

⁴ Quoted by Thomas.

and ileum; this has been noted also by several other observers. More recently Steiner¹ mentions a blotchy redness of the intestinal mucous membrane occurring in children dying during the eruptive stage.

According to Worthington,² the lymphatic follicles and Peyer's patches of the bowel may undergo destructive ulceration, leading even to perforation. Thomas says that Fuchs saw, upon the genital mucous membrane, numerous red, somewhat puffy spots overspread with mucus. This observation was likewise made by Henoch and Chomel.

Lymphatic Glands.—The lymphatic glands are enlarged in measles, but to a less extent than in scarlet fever. When bronchopneumonia is present the tracheobronchial glands may be found distinctly swollen. In a certain proportion of cases the glands show evidences of tuberculosis. Loomis, Pizzini, and Kalbe³ found tubercle bacilli in apparently normal tracheobronchial glands; the last-named observer noted the presence of these bacilli in 8 per cent. of apparently healthy glands. It is suggested that these lie dormant until an attack of measles or some other affection involving these glands stimulates the tuberculous process to activity.

Lungs.—Bronchopneumonia is present in a large proportion of the fatal cases. The process is not essentially different from that observed in bronchopneumonia independent of measles save that there is a more pronounced tendency in many cases to suppuration. It is not rare for the pulmonary trouble to eventuate in tuberculosis, exhibiting usually the form of a caseous pneumonia.

Cornil and Babes⁴ have described a peripneumonia which occurs early in the so-called suffocative cases, and which they regard as peculiar to measles. It begins in the lymphatic tissue, involves the interlobular and interalveolar structures, and leads to fibrinous exudation into the air vesicles.

Stiebel⁵ speaks of a blotchy redness of the pleural membranes which he observed in four autopsies. They were sharply contoured, red spots, apparently situated just beneath the pleura on both sides.

Roger observed a purulent pleurisy during convalescence from measles in a five-year-old child.

The *spleen* is moderately swollen in measles, although this is more often determined at autopsy than at the bedside.

Liver.—Freeman⁶ found focal necrosis of the liver in 4 out of 14 autopsies on measles cases. The larger areas of necrosis are visible to the naked eye and may be confounded with tubercle. Microscopically there is a sharply circumscribed roundish area of necrosis in which the cytoplasm fails to stain, and fragmentation of the nuclei is seen. The condition is due to the local action of bacterial toxins.

Blood.—In uncomplicated cases of measles the condition of the blood is unaltered. Fibrin may be increased when the catarrhal symptoms are severe.

¹ Quoted by Thomas.

² Mentioned by Roger, *loc. cit.*, p. 1004.

³ Quoted by Thomas, *loc. cit.*

⁴ Result of Work at the New York Foundling Asylum. *Archives of Pediatrics*, February, 1906, and *New York Medical Record*, 1898, vol. II.

⁵ Quoted by Dawson Williams.

⁶ Quoted by Williams, *loc. cit.*

The number of *red cells* is not strikingly reduced in mild or moderate cases, and may at times be actually increased. In 8 cases Felsenthal counted from five to five and a half million corpuscles. The hæmoglobin is likewise slightly or not at all reduced.

The *white cells* not only are not increased in measles, but they are often reduced below the normal. In 8 cases Rieder noted an average of 7500 cells, the leukocytes being least numerous at the height of the disease, and increasing as the fever disappeared. Cabot¹ states that during convalescence the lymphocytes and especially the large mononuclear forms are increased.

According to Coombe, uniform changes occur in the blood in the incubation period. Coombe² says: "In the incubation period of measles there is a hyperleukocytosis without other symptoms. This is a constant sign of the incubation period. During the last two days of the period of invasion or exanthem, and throughout the entire period of the exanthem, there is a *hypoleukocytosis*."

These alterations are due to the change in the number of the polymorphonuclear neutrophils. These observations were confirmed by Platenga,³ who also found similar changes in rubella.

The eosinophile cells are usually decreased or normal in number. Cabot found the differential counts normal; Felsenthal found the polymorphonuclear cells much increased and eosinophiles never over 1 per cent.

In cases in which the *diagnosis* between scarlet fever and measles is obscure, a differential blood count should be of distinct value. On the other hand, the examination of the blood is of no particular value in differentiating measles from rubella (*rötheln*), inasmuch as the cellular constituents are much the same in the two diseases.

THE BACTERIOLOGY OF MEASLES.

The extreme contagiousness of measles is proof of its microparasitic origin; some reservation must, however, still be expressed as to the etiological relationship of the organisms thus far described.

Braidwood in 1878 called attention to a bacillus which he found in measles and which he regarded as the cause of the disease. Lombroso⁴ described cocci in the rete mucosum of the measles spots. Similar bodies were found by von Leyden and Fürbringer.

In 1892 Canon and Pielicke found in 14 cases of measles a bacillus which they considered to be the specific causative agent. The discovery was made possible by a special method of staining.⁵ The organism was variable in size, sometimes quite small and resembling a diplococcus,

¹ Clinical Examination of the Blood, fourth edition, New York, 1901.

² Archiv. de méd. des enfants, 1903.

³ Archiv. de méd. des enfants, March, 1903.

⁴ Lo Sperimen., 1884, x.

⁵ Stain for the bacillus of Canon and Pielicke. Blood is thinly spread upon a clean cover-glass and fixed by five to ten minutes' immersion in absolute alcohol. Then stain with the following solution and incubate at 37° C. for from six to twenty-four hours: Concentrated aqueous solution of methylene blue, 40; 0.25 per cent. solution of eosin in 70 per cent. alcohol, 20; distilled water, 40.

and other times as long as a red blood cell. It was present in the blood, sputum, and secretions of the nose and eyes throughout the entire disease, but disappeared when convalescence set in. The bacillus could be grown on bouillon, but on no other media.

Czajkowski¹ found a bacillus in the blood and mucous secretions of 50 cases of measles, which was apparently identical with that above described. It grew, however, on various albuminous media, especially blood serum and glycerin agar, but not on gelatin and plain agar. Inoculations of mice produced a fatal septicæmia. Gregorieff, in an examination of the blood in 13 cases, found the bacillus in each case, and grew it in bouillon in 10 instances.

Josias² failed to find this organism in a study of the blood and secretions of 24 cases, and Barbier and Warschovsky also obtained negative results, the latter examining 21 cases.

Arsamakov,³ in an examination of 665 cases of measles, found in the blood and mucous secretions, grouped, rod-shaped bodies, 5 to 6 microns in length, having bulbed extremities.

In 1900 Lésage⁴ published the results of a study of 200 cases of measles. He found a delicate micrococcus which grew best on gelose (agar), took stains slowly, and was decolorized by Gram's method. The cultures bore a resemblance to those of the pneumococcus. The organism was found constantly in measles, but was absent in 25 cases of scarlet fever and in 45 normal children. In 53 children who had had measles previously it was found twice. Rabbits were inoculated with blood and nasal secretions in many cases, and measles apparently reproduced in nearly all.

Von Niessen⁵ examined the blood during the height of the measles exanthem and found a bacillus which in some respects resembled that of Canon and Pielicke. It produced, however, rose-colored colonies on gelatin and grew well also on glycerin agar, bouillon, and potato. He designated this organism "bacillus roseus."

In 1891 Doehle⁶ found in the blood of 8 cases of measles certain bodies which he regarded as protozoa. In fresh blood they were observed not only in the plasma, but also in the red blood corpuscles. After the eruption appeared the bodies became visible almost exclusively in the red cells. They were from a half to one micron in diameter and exhibited an opaque nucleus with a surrounding clear zone. Later larger oval bodies with two nuclei were seen.

More recently Weber⁷ has detected bodies in the blood which he regards as protozoa. From the above divergent findings it is evident that further research is necessary before any of the organisms described can be accepted as the specific cause of measles.

¹ *Centralbl. f. Bakt. u. Parasit.*, 1895, Nos. 17 and 18.

² *La médecine moderne*, Paris, June 2, 1902.

³ Article abstracted in *Revue de médecine*, 1899, vol. xix, p. 561.

⁴ *Bulletin de la Société des hôpitaux de Paris*, March 15-22, 1900.

⁵ *Arch. f. Derm. u. Syph.*, 1902, vol. lx, p. 429.

⁶ *Centralbl. f. allgem. Path.*, etc., 1892, lili, p. 150.

⁷ *Centralbl. f. Bakt. u. Parasit.*, 1897, vol. xxi, p. 296.

THE DIAGNOSIS OF MEASLES.

It is a matter of great importance, particularly in institutions for children, that the diagnosis of measles be made at as early a date as possible in order that the spread of the infection may be prevented. Unfortunately the contagium of measles is transmitted at a very early period, not infrequently on the first or second day of the invasive illness, and before the diagnosis is firmly established. The existence of an epidemic of measles or knowledge of exposure to the disease will put the physician on guard and often enable him to make a diagnosis, or at least strongly suspect it, upon the first development of catarrhal symptoms. The statement is equally true of measles and smallpox, that the diagnosis cannot be indubitably made before the appearance of the eruption, although when all of the invasive symptoms are typically developed, when there has been exposure to the disease, and, particularly when the characteristic buccal enanthem is present, the diagnostic probability approaches almost to a certainty. As in smallpox, the vaccinal condition of the patient often constitutes information of important diagnostic value, so in measles does the history as to previous attacks. It is generally agreed that second attacks of measles are of great rarity. In a doubtful case, an authentic history of a previous attack, of measles would constitute strong presumptive evidence against the rubeolous nature of the disease under consideration.

While the diagnosis of measles is usually announced when the eruption appears, it must not be thought that the rash is in itself all-sufficient evidence.

The eruption of measles is merely its most conspicuous manifestation. Rashes indistinguishable from the measles exanthem may, at times, appear in other diseases. The diagnosis is to be made by attention to the history, the catarrhal symptoms, the fever, and the eruption, both upon the skin and buccal mucous membrane. A due sense of proportion must be cultivated so that the presence or absence of certain symptoms may be accorded its proper value.

Ordinarily the diagnosis of measles presents no difficulties. When, however, the disease appears in unusual guise, in extremely mild or malignant or irregular form, the determination of the nature of the disease may be most perplexing. Especially is this true in those rare cases of *measles without eruption*; in such instances the diagnosis can only be made when the history and the entire clinical picture, save the eruption, bespeak measles.

Diagnostic Value of the Enanthem or Mucous-membrane Eruption (Koplik's Spots).—It is stated by Northrup¹ that the typical buccal spots are present in measles in about 91 per cent. of cases, that they are seen only in measles, and that they ordinarily appear from one to three days before the cutaneous eruption.

Our own experience would confirm this statement. We have observed

¹ Von Jürgensen's article on Measles in Nothnagel's Encyclopedia of Practical Medicine, American edition; additions by Northrup.

the spots as early as three days before the appearance of the cutaneous exanthem. We have never seen these spots in rubella, scarlatina, or any other disease save measles.

Rotch, of Boston, reflects the general opinion in the following statement: "The presence of Koplik's spots helps in a large majority of cases. The consensus of medical opinion appears to be that while their absence does not exclude measles, their presence is pathognomonic of measles."

Sevestre¹ insists upon the diagnostic importance of the erythema of the soft palate which precedes by one or two days the exanthem of measles. "The redness is not uniform, but presents itself in the form of small, rounded or irregular spots, which are sometimes disseminated in small number and at other times almost confluent." This appearance of the soft palate to our minds is scarcely sufficiently peculiar to measles to be of much diagnostic value.

It is at times a matter of importance to determine during convalescence the nature of the preceding disease. Measles may often be diagnosed by the brownish-red stains on the body as late as a week or ten days after the subsidence of the eruption. Inasmuch as children in this condition may be capable of transmitting the infection, it is important in schools, asylums, or other institutions for children to exclude or isolate such patients. Not infrequently a mild grade of blepharitis persists after an attack of measles.

Rubella (Rotheln).—This affection is more apt to be confounded with measles than any other. Confusion may arise when measles presents itself in very mild form or when rubella appears, as it sometimes does, with severe manifestations. The history as to the previous occurrence in the patient of the one or the other disease is evidence of considerable importance. It is uncommon for measles to attack an individual twice and still rarer for rubella to act in this manner.

The prodromal stage in rubella is very brief, rarely lasting more than twenty-four hours; the catarrhal symptoms are slight or absent. It will be helpful to remember that catarrhal manifestations are more pronounced in mild cases of measles than in severe cases of rubella. The characteristic buccal spots seen in measles are absent in rubella. The fever is slight, commonly 99° or 100° F., and rarely exceeding 101° F.; it is of short duration. The eruption in rubella spreads more rapidly than in measles and is of briefer duration. The lesions are slightly elevated macules, of a pale rose-red color, and pinhead to pea sized. The eruptive elements are smaller, paler, and more discrete than in measles. The patient with rubella often feels well enough to remain out of bed. A more exhaustive differential diagnosis is given in the chapter on Rubella.

Scarlet Fever.—It is only in anomalous cases that scarlatina is apt to be confounded with measles; ordinarily the differentiation of these affections is a simple matter.

¹ Quoted by Comby, p. 195, loc. cit.

In scarlatina the onset is more stormy, with high fever and a much greater tendency to vomiting. The eruption usually comes out on the second day, earlier therefore than that of measles. Photophobia, coryza, hoarseness, and cough are lacking in scarlatina, but instead we find sore throat, marked glandular enlargement about the jaws, and a characteristic tongue. The peculiar buccal spots of measles are absent, the oral and pharyngeal mucous membrane showing merely congestion. The face is less intensely involved by the rash than in measles and, moreover, shows circumoral pallor.

The rash in scarlet fever is diffuse and punctiform; it should be remembered, however, that on the arms and legs it is not infrequently blotchy and suggestive of measles. The subsequent desquamation is more profuse and lamellar in character. Otitis media and albuminuria are common complications. In septic cases purulent nasal discharge is not uncommon even in the early stages of the disease; laryngeal symptoms are, however, rare.

Confusion may result in those cases of measles in which there is a tendency to general confluence of the rash; usually some portions of the cutaneous surface will exhibit the measly character of the rash. In patients seen late brownish stains on the body speak for measles, and pronounced desquamation on the hands and feet and albuminuria point toward an antecedent scarlet fever.

Influenza.—"La grippe," particularly that form accompanied by catarrhal inflammation of the upper air passages, may present a considerable resemblance to measles during the invasive stage. It is manifest that a disease beginning with fever, coryza, and cough might readily be either measles or influenza. Photophobia, which is justly regarded as a significant symptom by the laity, is usually well marked in measles and absent in influenza. If the characteristic bluish-red spots with whitish specks on their summits be visible upon the buccal mucous membrane the diagnosis is at once made clear.

The presence of an epidemic of one or the other disease will often aid one in early arriving at a correct diagnosis.

Smallpox.—During epidemics of smallpox, cases of measles are not infrequently confounded with variola. We have had numerous cases of measles sent into the Municipal Hospital under the diagnosis of smallpox. On the other hand, the reverse error is by no means rarely made. It is particularly the severe cases of smallpox with considerable turgescence of the skin that simulate measles. Standing some feet from the patient the resemblance in these cases is striking. Some cases of measles are accompanied by a considerable degree of papulation; when such an eruption is developed by an adult during an epidemic of smallpox, an error might at the very beginning be readily made (Fig. 87). A further point of resemblance is that each disease is preceded by a prodromal stage of almost the same duration.

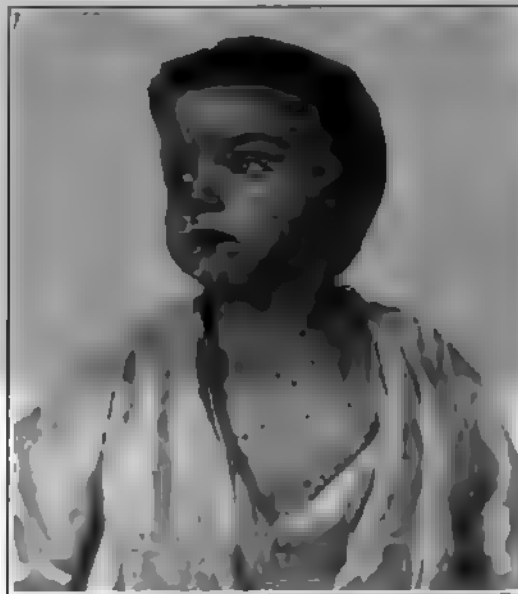
The constitutional symptoms preceding smallpox are, however, usually more severe (temperature 104° to 105° F.), and are commonly, though not always, accompanied by pronounced backache. The

temperature, moreover, falls a few days after the appearance of the eruption, while the fever in measles continues high during the eruptive stage.

The catarrhal symptoms affecting the eyes and respiratory passages, which are so constant in measles, are absent in smallpox, at least during the prodromal stage. Close inspection of the mouth in smallpox may reveal the presence upon the soft palate of rounded, glistening, pinhead-sized, reddish elevations, but these differ considerably from the bluish-red spots on the buccal mucous membrane in measles.

The maculopapules of measles are soft and velvety to the touch, as compared with the firm, shotty character of the smallpox papules.

FIG. 87



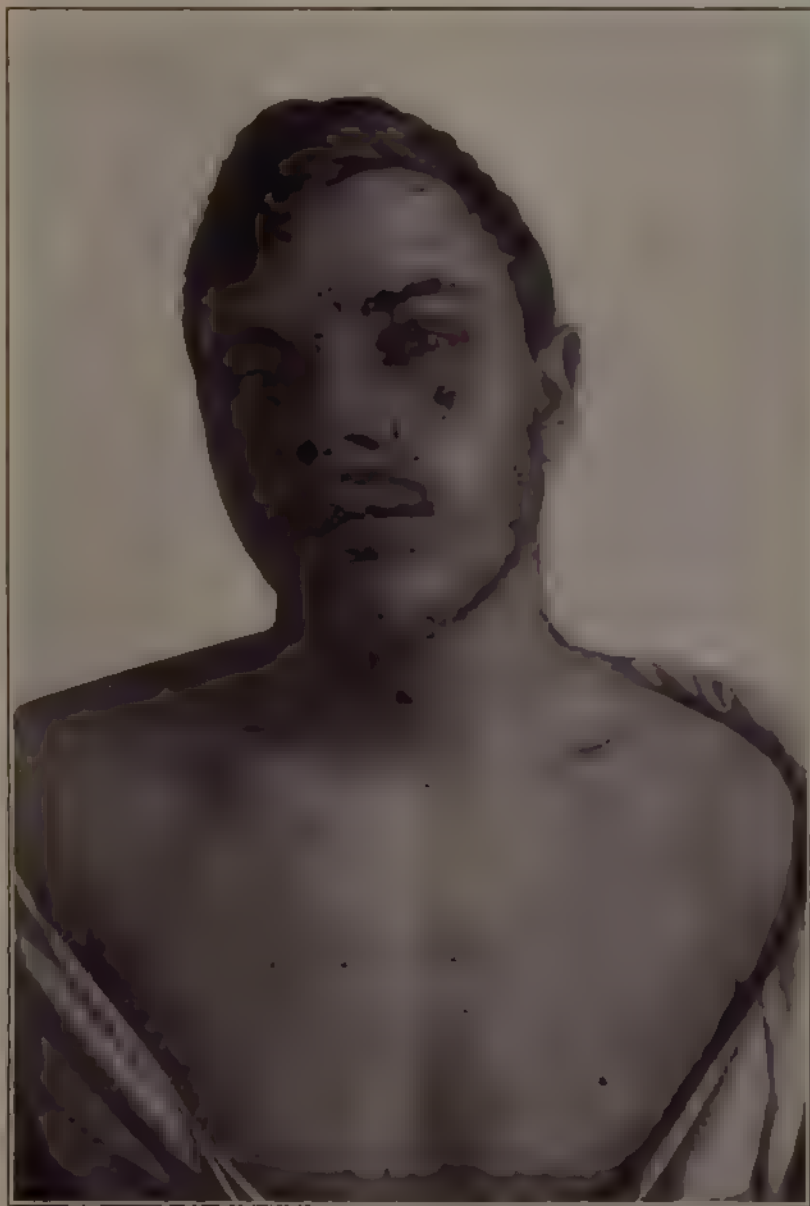
Smallpox on the second day of the eruption, presenting some resemblance to the eruption of measles.

The sweep of an experienced hand over the skin will often suffice to differentiate the two diseases. Where there is doubt, twenty-four hours' delay will dispel all uncertainty, for by this time the eruption of measles will have become flatter and more diffuse, and the papules of smallpox firmer and more distinctly elevated.

The prodromal morbilliform rash, the so-called *roseola variolosa*, may be confounded with measles. This eruption occasionally develops in mild cases on the second day of the invasive stage. The lesions are non-elevated, irregular in distribution, of brief duration, and unaccompanied by catarrhal symptoms.

Typhus Fever.—During the epidemic prevalence of typhus a confounding of this disease with measles might take place when the eruption

PLATE LI.



Measles with Papular Lesions, sent into the Municipal Hospital
as a Case of Smallpox.

is profuse. Pastau is quoted by Thomas as saying that the exanthem of typhus is by no means rarely papular or even hemorrhagic like that of measles, and a catarrhal affection of the air passages, especially of the trachea, is one of its usual concomitant symptoms. The fever and nervous symptoms are more pronounced in typhus and there is great enlargement of the spleen; the eruption is usually absent on the face, and oculonasal catarrh is lacking. We recall a case of atypical measles which was sent to the Municipal Hospital as a case of typhus by one of the foremost physicians of this country.

Roseola Syphilitica.—The macular eruption of syphilis has on more than one occasion been confounded with measles. The error of mistaking syphilis for measles may be made when the patient is an adult and when the febrile symptoms are mild. On the other hand, syphilis with pyrexial elevation might be regarded as measles.

The eruption of syphilis is slower in development and the lesions are much more uniform in size and distribution. The face is but slightly, if at all, involved. Usually the initial lesion or the hardened remains thereof can still be discovered. In addition other evidence of the syphilitic infection may be present, such as mucous patches, pronounced inguinal adenopathy, etc.

Morbilliform Erythemata.—There are a number of conditions in which rashes bearing a more or less close resemblance to that of measles may occur. They may be divided into: (a) accidental rashes accompanying the exanthematous fevers, (b) drug eruptions, and (c) serum eruptions.

Mention has already been made of the resemblance of the roseola variolosa to measles. An analogous eruption, *roseola vaccinosa*, develops occasionally about the tenth day of vaccination. The same features which have been referred to as distinguishing the variolous roseola from measles may be applied to the vaccinal rash. Morbilliform rashes may in rare instances be observed also in the course of varicella, scarlet fever, and other infectious diseases.

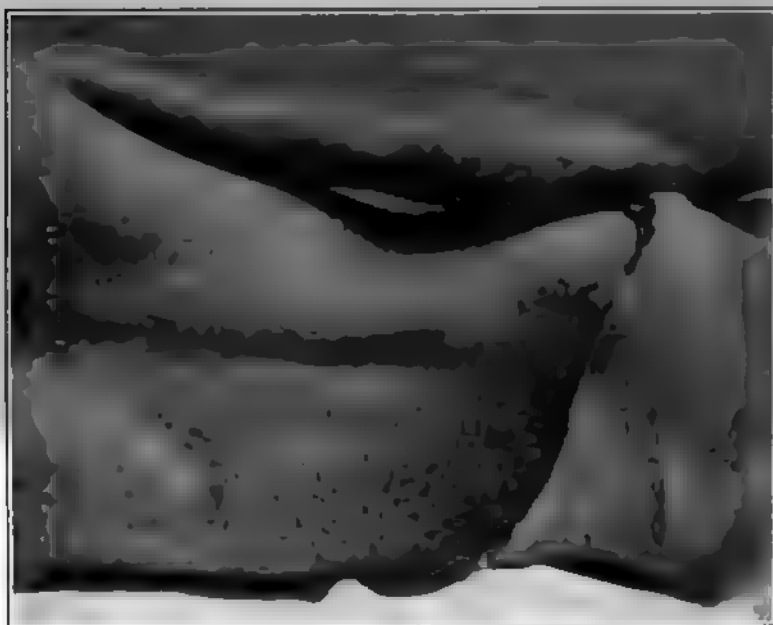
Drug Eruptions.—The drugs which most frequently give rise to eruptions simulating measles are antipyrin, quinine, chloral, copaiba, and cubebs.

The most common eruption resulting from the administration of *antipyrin* is a morbilliform erythema. Of 52 instances of eruption from the use of antipyrin collected by Spitz, 41 were of the measles type. The eruption may be generally distributed over the trunk and extremities or it may be limited to certain regions thereof; an important distinguishing feature is that the face is usually exempted. Croker states that these eruptions may be accompanied by oronasal catarrh. The difficulty in diagnosis may be increased by the appearance of the antipyrin eruption following catarrhal symptoms, such, for instance, as are encountered in influenza, for which the drug is administered. The conjunctivitis, photophobía, hoarseness, cough, and buccal eruption are all absent. Fever, when present, is slight and not characteristic of measles. Furthermore, the normal progression of the measles exanthem from the

face and neck gradually downward will be found lacking. The eruption, moreover, is apt to be non-elevated and exhibit irregularities as to distribution. If a large dose of antipyrin has been taken the drug can be found in the urine by testing the same with the perchloride of iron.

QUININE.—Quinine gives rise not infrequently to erythematous eruptions. Of 60 quinine eruptions analyzed by Morrow, 38 were of the erythematous variety. Most of these are of the scarlatiniform type, but some resemble measles. The rash may develop after the administration of as small a quantity as a grain or even a fraction of a grain of the drug. The idiosyncrasy appears to be most frequently observed in women.

FIG. 58



A morbilliform erythema somewhat resembling measles, probably due to intestinal autointoxication.

The eruption may be generally distributed or limited to certain areas. It sometimes appears first on the face, spreading thence downward over the trunk and limbs. The lesions are bright or dull red macules or papules, which may quite strongly resemble the measles exanthem. Itching is apt to be a more prominent symptom than that accompanying measles. Desquamation not infrequently follows. In some cases febrile symptoms are present at the beginning; there may be a fever of 101° or 102° F., with headache, nausea or vomiting, and weakness. Catarrhal symptoms are absent.

Eruptions from the administration of *chloral* are less common than those after antipyrin or quinine. Gee¹ saw two cases in which there was

¹ Quoted by Crocker, *Diseases of the Skin*, American edition, 1903, p. 423.

a dusky-red, papular eruption surrounded by a more diffuse redness of the face and neck, and patchy or mottled-red spots on the extremities, especially about the articulations.

The absence of the catarrhal and constitutional manifestations of measles would enable one to exclude this infection.

COPABIA and CUBEBS.—Copaiba and cubebs may give rise to scarlatiniform or morbilliform rashes. The former drug usually produces an eruption consisting of rose-red colored, slightly raised patches, which may be discrete or blotchy and generalized or limited. About the elbows and knees there is a tendency toward confluence of the patches. Itching is apt to be a distressing symptom. The eruption may develop rapidly after the administration of the drugs or only after some days have elapsed. Most of the eruptions have occurred in persons who were receiving treatment for urethritis. A peculiar and disagreeable balsamic odor is often imparted to the skin when copaiba is taken.

All of the drug eruptions are apt to exhibit irregularities as to the manner, rapidity, distribution, or duration of the eruption which will arouse suspicion as to its nature; furthermore, the prodromal stage of measles with its characteristic catarrhal symptoms is wanting.

ANTITOXIC SERA.—Antitoxic sera occasionally call forth eruptions which are measles-like in character. Diphtheria antitoxin may now and then give rise to a morbilliform erythema, although much more commonly the eruption resembles urticaria or exudative erythema. Antitoxin rashes may develop at any time from three days to three weeks after its administration; most rashes, however, appear from eight to fourteen days thereafter. There may be elevation of temperature with joint pains and occasionally joint swellings accompanying the eruption. The temperature may rise suddenly to 102° F. or thereabouts, but it soon falls. Catarrhal symptoms are invariably absent.

The antistreptococcus serum and antitetanic serum may, on rare occasions, also give rise to morbilliform eruptions.

THE PROGNOSIS OF MEASLES.

It appears to be a difficult matter to dispel from the minds of mothers the idea that measles is a trivial disease. When it is stated, according to the *Twelfth Census Report*, that measles in the United States, in the year 1900, caused 12,866 deaths, more than twice the number that resulted from scarlatina, it is evident that this disease is not essentially benign in its outcome. The above statement must not be construed to mean that measles is more dangerous than scarlet fever, but that, attacking as it does a much larger percentage of humanity, the aggregate loss of life is greater.

The prognosis of measles in vigorous and well-nourished children beyond the age of two or three years is extremely favorable.

The factors that exert an important influence upon the prognosis are the age of the patient, his previous health, and the nature of his surroundings. Season and climate are thought to exercise some influence upon the disease and its complications.

Age.—The age of the patient is the most important factor in estimating the degree of danger attendant upon an attack of measles. During the first six months of life infants usually resist the infection of measles altogether or take it in feeble form. With this exception, children under two years of age who contract measles have a dangerous disease to contend with. Holt states that the average mortality from measles during this period is not far from 20 per cent.

After the third year of life the danger rapidly diminishes, reaching a minimum after the age of five has been passed.

The following figures of Tripe¹ indicate the relation of age to mortality.

Mortality of Measles in England from 1868 to 1872.—In 1000 fatal cases the age of the patients was:

0-1 year	200 cases.	5-15 years	72 cases.
1-2 years	376 "	15-25 "	3 "
2-3 "	190 "	25-45 "	4 "
3-4 "	101 "	45-60 "	1 case.
4-5 "	58 "	Over 60 "	0 "

It is thus seen that about three-quarters of the deaths occurred in children under three years of age.

Dawson Williams states that in the forty years from 1848 to 1887 there were in England and Wales 367,602 deaths attributed to measles, and of this number 335,874 occurred in children under five years of age, leaving only 31,728 to distribute among other ages.

The best opportunity of judging of measles susceptibility and fatality at the various ages is afforded in studying an entire epidemic in a locality. Dr. Theodore Thomson² presents such a table of an epidemic in an English town, from which the following data are abstracted:

Age.	Population.	Measles attacks.	Deaths.	Mortality rate.
0-1 year	1155	166	16	9.9 per ct.
1-2 years	974	233	46	23.6 "
2-3 "	1023	354	36	17.5 "
3-4 "	1000	324	16	8.0 "
4-5 "	961	324	5	2.6 "
5-10 "	4530	560	6	0.7 "
10 years and upward	25,968	39	0	0.0 "
At all ages	38,608	1031	126	1.7 "

This table indicates the lesser susceptibility of infants under one year of age and also the lower death rate as compared with the next two years.

During youth and early adult life the mortality from measles is low. Patients who are advanced in years not infrequently succumb to the disease. This is shown in Panum's³ report of the Faroe Islands epidemic of 1845.

¹ Quoted in *Jahrbuch f. Kinder.*, vol. ix p. 412.

² Loc. cit., p. 287.

³ Quoted by Williams, loc. cit.

MORTALITY RATE OF MEASLES IN THE FAROE ISLANDS IN 1845.

Age.	Mortality rate.	Age.	Mortality rate.
Under 1 year	. 80.0 per ct.	40-50 years	. . 2.8 per ct.
1-10 years	. . 0.6 "	50-60 "	. . 4.5 "
10-20 "	. . 0.4 "	60-70 "	. . 7.8 "
20-30 "	. . 0.75 "	70-80 "	. . 13.1 "
30-40 "	. . 2.1 "	80-100 "	. . 26.1 "

These figures are unusual in that such a great mortality is shown in infants under one year of age and such a remarkably small death rate in those between one and three years. The increasing mortality in patients past the age of forty is well illustrated. In an extremely mild epidemic in the Faroe Islands in 1875, Hoff states that while only 8 out of 1123 cases ended fatally, 5 of these were vigorous adults between the age of twenty and thirty years. This must be regarded as an exceptional circumstance.

Institutional Epidemics.—It will be found convenient to discuss here the influence of institutional environment upon the mortality rate of measles. It is a generally recognized fact that measles occurring among children in homes, nurseries, asylums, hospitals, etc., is much more fatal than when it develops among children in their private homes. Indeed, measles is regarded as the scourge of children's institutions, for it decimates the little patients like a plague. There are a number of reasons for this. Such children usually come from poor stock and therefore lack power of resistance. The children in foundling asylums, nurseries, and hospitals are of a tender age, which in itself accounts for a high mortality. They are usually frail and in poor health or already perhaps suffering from an acute or a chronic disease. The atmosphere is often vitiated and infected and the liability to such complications as pneumonia and diphtheria is increased.

The mortality in such institutions as have been mentioned is often frightful. Holt speaks of an epidemic in 1892 in the Nursery and Child's Hospital in New York in which there were 143 cases with a death rate of 35 per cent. An epidemic in the same institution in 1895 had an almost identical mortality rate.

Comby gives the following statistics showing the death rate in some of the Paris hospitals:

HÔSPICE DES ENFANTS ASSISTÉS.

Year.	Cases.	Deaths.	Percentage.
1882	280	128	45.0
1883	268	128	47.0
1884	328	187	57.0
1885	370	147	46.0
1886	229	138	42.0
Total in five years	1575	728	46.22

The death rate, therefore, during these five years was nearly 50 per cent., a truly appalling figure.

In l'Hôpital des Enfants Malades, for a period of seven years from 1882 to 1888, there were treated 2585 cases of measles, with a death rate of 40.15 per cent.

In l'Hôpital Trousseau, from 1882 to 1886, there were 907 cases of measles, with a mortality rate of 25.02 per cent. From 1890 to 1894 there were 2248 cases treated in special isolation pavilions, but the mortality rate still remained high—28 per cent.

It is difficult to obtain accurate information as to the death rate of measles in private practice, for while the deaths are recorded the number of attacks is usually not known. The fact is well established, however, that the fatality is very much less in this class of patients.

Sex does not influence the mortality from measles. Of 12,866 persons who died of measles in the United States in 1900, 6231 were males and 6635 were females. The frequency of measles in pregnant women is not sufficient to disturb the balance. Moreover, the infection of measles superadded to pregnancy is not as serious as some of the other exanthematous diseases, notably scarlet fever and smallpox.

Previous Health of the Patient.—Measles as a primary disease is very much less serious than when it becomes engrafted upon some other acute or chronic affection. Secondary measles is an extremely fatal disease; occurring in patients who are convalescing from diphtheria, scarlet fever, whooping-cough, etc., the danger is greatly enhanced.

The mortality is also high when measles attacks children who are badly nourished and who are scrofulous or anemic. In those with enlarged glands and a tendency to pulmonary tuberculosis an attack of measles may be sufficient to stimulate this process into activity. The unfavorable influence of hardship and privation is exemplified in camp measles, which is nearly always characterized by a high death rate.

Character of Epidemic.—The mortality of measles depends much upon the severity of the prevailing epidemic. At times the type of measles is unusually mild and the death rate extremely low; some epidemics, on the other hand, are characterized by special malignancy. Fatal epidemics of measles may cause a high mortality, not only through an excessive development of the regular symptoms of the disease, but through the frequency of serious complications. Indeed, it is the frequency or rarity of bronchopneumonia during an epidemic that determines in a large measure its malignancy.

The average mortality of measles is from 4 to 6 per cent. The deaths may in some epidemics not exceed 1 or 2 per cent., while in others they may reach the murderous figures of 20 or 30 per cent.

In 1856, in Lippe, Hungary, a malignant epidemic prevailed, destroying the lives of 50 per cent. of those attacked. Measles again occurred in this locality thirteen years later, with a mortality of 3 per cent.

Faber states that at Schorndorf in the epidemic of 1827-28 there were 2100 cases of measles, with a mortality of only 1.8 per cent. Among other mild epidemics may be mentioned the following, quoted by Thomas: According to Ranke the mortality in four epidemics in Munich varied from 0.7 to 2.7 per cent. Kostlin reports a mortality in Stuttgart of 1.8 per cent. for the years 1852 to 1865.

Among severe epidemics (according to Thomas) may be mentioned the fatal epidemic in the district of Zolkiew in 1840; Seidl mentions that

out of 1519 cases there were 196 deaths, a mortality of almost 13 per cent. According to Schüz measles prevailed at Nagold with a mortality of 10 per cent. Small epidemics in certain localities have been accompanied by even higher mortality.

Colin¹ gives the following figures:

Year.	Localities.	Cases.	Deaths.	Percentage.
1861	Ruelle	582	139	27.7
1864	Arras	45	18	28.8
1860	Val-de-Grace	125	40	32.0
1870	Bicêtre	457	168	36.7

A malignant epidemic raged in Sunderland, England, in 1885. Harris² states that of 1316 cases 384 died, giving a mortality of 29 per cent.

Measles often manifests unusual malignancy on reaching a virgin soil, particularly among savage tribes. It is stated on the authority of d'Alves that 30,000 Indians perished from measles along the banks of the Amazon River in 1749-50. In 1806, in Madagascar, 5000 persons are said to have succumbed to the disease in a single month. Among the Fiji Islanders measles has exhibited as high a death rate as 30 per cent.; the disease has, as might be expected, inspired a wholesome dread among the natives.

Season and Climate.—Inasmuch as the mortality of measles is greatly influenced by the frequency of pneumonia, one would naturally suppose that this complication would be more common and the death rate consequently higher in the cold and inclement seasons of the year. But such an assumption is not entirely borne out by facts. The figures which are published by writers as to the influence of season on measles mortality lack uniformity and preclude the possibility of drawing therefrom satisfactory conclusions.

DEATHS FROM MEASLES IN ENGLAND AND WALES BY QUARTERLY PERIODS.

Quarterly Periods.	1837.	1838.	1839.	1840.
January, February, and March	2022	2074	2836
April, May, June	1512	3204	2641
July, August, September	2362	1037	2767	1739
October, November, December	2392	1943	2892	2110
Total deaths	4754	6514	10,937	9326

Gregory, who publishes the above table, remarks that “season would appear to have less influence on the mortality of measles than might have been anticipated.”

According to Karajan,³ measles occurring in lower Austria in 1862, during the presumably unfavorable cool months, was attended with a mortality of only 2.29 per cent., whereas the disease prevailed in the same district during the following summer with a mortality which reached 6.29 per cent.

Passow⁴ states that the fatal cases of measles in Berlin from 1863 to

¹ Quoted by Comby.

² Lancet, April 30, 1887, p. 970.

³ Quoted by Thomas.

⁴ Quoted by Thomas.

1867 were distributed as follows: winter, 41.4 per cent.; autumn, 33.4 per cent.; summer, 13.3 per cent.; spring, 11.9 per cent.

In the United States the most fatal season from measles would appear to be the late winter and early spring months.

In the city of New York, during a period of fifteen years from 1830 to 1844, in which time 2104 deaths from measles occurred, the seasonal mortality was as follows:

January, February, March	610 deaths.
April, May, June	574 "
July, August, September	536 "
October, November, December	394 "

It is thus seen that the highest mortality was in the first three months of the year and the lowest in the last three.

The *United States Census Report* for the year 1900 shows that the greatest number of deaths from measles occurred during the months of February, March, April, and May.

COMPARATIVE PROPORTION OF DEATHS IN EACH MONTH PER 1000 DEATHS
IN THE UNITED STATES FOR THE YEAR 1900.

January	95.0	July	48.5
February	150.1	August	43.6
March	176.0	September	34.7
April	146.8	October	25.6
May	130.3	November	34.6
June	66.4	December	48.6

Climate doubtless has some influence upon the mortality of measles. Gregory says that "in hot countries measles is not viewed with alarm, evidently from the absence of thoracic complications." It occurs to us, however, that the greater tendency to intestinal complications might counterbalance the advantage. The mortality of measles varies in different localities. It is, as would be expected, greater in large cities, where there are greater numbers of overcrowded poor than in rural districts. Even in large capitals a considerable discrepancy in the mortality exists.

Thus the mortality from measles is much greater in London than in Berlin; this is strikingly shown by the following figures:

MEASLES DEATHS PER 10,000 OF POPULATION.

Year	Paris.	London.	Berlin.	Vienna.
1880 to 1889	52	60	30	60
1890 " 1894	41	77	20	70
1895	26	59	17	49

From a consideration of the above remarks it will be seen that many factors influence the prognosis; chief among these, however, are the age of the patient, his general health and environment, and the severity of the epidemic. Those epidemics which furnish the largest number of anomalous cases and the greatest percentage of serious complications are most to be feared.

Bronchopneumonia causes nine out of ten deaths from measles. It is the principal danger to which measles patients are liable. Holt states

that of 51 fatal cases of measles 45 were due to bronchopneumonia, 4 succumbed to ileocolitis, and 2 to membranous laryngitis.

Among 36 deaths observed by Northrup,¹ in an epidemic in the New York Foundling Hospital, bronchopneumonia was found *post-mortem* in 31 cases.

Favorable Symptoms.—The symptoms of measles are favorable when the initial temperature is moderate, not exceeding 103° F., and when it remits in the pre-eruptive stage; when the temperature declines with the beginning fading of the eruption; when the eruption is discrete, well developed, and of bright color; when it appears about the fourth day and progresses gradually over the body; when the catarrhal symptoms are of moderate intensity; when complications are absent.

Unfavorable Symptoms.—It is unfavorable for the initial temperature to be very high (above 103° F.), or for it to persist high or increase before the eruption appears. It is ominous for the fever to remain high after the rash fades, for this usually portends pulmonary complications. It is unfavorable for the eruption to appear late, for it to be unusually profuse or confluent or, on the other hand, sparse, pale, and livid. A partial or poorly developed eruption with high fever is a bad sign. Hemorrhagic eruptions are usually of evil portent, especially when accompanied by hemorrhages from the mucous membranes. Sudden and premature recession of the eruption indicates cardiac weakness. Convulsions or other marked nervous symptoms, severe diarrhoea, persistent hoarseness, with difficulty in breathing or continued high temperature, indicate serious complications.

THE TREATMENT OF MEASLES.

In discussing the treatment of measles it must be remembered that we are dealing with a disease which is far from trifling in its nature—one whose aggregate annual mortality exceeds, at the present day, that of any eruptive disease, not excluding smallpox. In 1889 there were 14,732 deaths from measles in England and Wales; in 1900 the mortality from measles in the United States was 12,866. These figures are not far from representing the average annual mortality in these countries.

We have no doubt that at least 100,000 persons, chiefly children, perish throughout the world each year from measles.

The subject is, therefore, of sufficient importance to warrant a full consideration of the *prophylactic* treatment of measles and its relation to the community at large.

Prophylaxis—That the spread of measles can be greatly lessened by proper sanitary measures has been shown by the results accomplished by the Michigan State Board of Health.² Public health measures may be considered under the headings of (1) Notification, (2) Isolation, and (3) Disinfection.

¹ Medical News, 1897, vol. lxxi. p. 817.

² Baker, Reports and leaflets on the Prevention and Restriction of the Infectious Diseases, etc., 1900.

Notification.—There is considerable difference of opinion as to the benefits derived from making measles a notifiable disease. Bearing in mind the fact that measles in many countries kills more children than scarlet fever and diphtheria combined, there can be but one point of view as to the desirability of checking its ravages. It is only through a knowledge of the distribution and extent of measles that health authorities are enabled to direct measures against its spread. How effective such measures are offers latitude for discussion.

The chief difficulty arises from the early communicability of the disease. As soon as a patient manifests the first symptom of measles, those who have been exposed and are susceptible are almost sure to contract the disease, and isolation, as far as these persons are concerned, is too late. Infection may at times take place even before the patients sicken, as is illustrated in the following cases mentioned by Dr. Fenton, Medical Officer of Health for Coventry, England:¹ "Thirteen children attended a dancing class one afternoon, including 3 of my own and 2 of a friend, who had just arrived in the district, and who had been exposed to the infection of measles before arriving. These 2 children came to my house and spent the evening in my presence. There was nothing to attract my attention to their condition, and, indeed, so well were they that they had walked six miles in the morning, had danced in the afternoon, and walked home about one mile at night. Next day they both sickened and developed measles. Of the remaining 11 children 2 were presumably immune, having previously suffered from measles, but the whole of the 9 developed measles during the following fourteen days." This incident is evidence of the early contagiousness of measles and the difficulties that are encountered in preventing its dissemination. But much can be accomplished in preventing unnecessary exposure to the disease, and to this end notification is eminently desirable, if not essential.

The *education of the masses* is a matter of paramount importance in stamping out measles. Mothers must be taught that measles is a serious disease—a disease that destroys many lives, and that exposure to it must be avoided. Even among the intelligent middle classes there is a tendency to regard escape from measles as futile, and mothers make little effort to avoid an infection which is regarded after all as inevitable. "The baby might as well take measles now as later" is the dangerous and erroneous view often expressed.

Mothers should be made to realize the fact that measles kills more children under two years of age than any other disease save possibly whooping-cough, and that about 80 per cent. of all deaths from measles are in children under five years of age. If children be safely guarded through this period of their life without contracting measles an enormous saving of life would result.

It is a good plan to send circulars of instruction to all households which are in the neighborhood of an infected domicile.

¹ Quoted by Dawson Williams.

Isolation.—When a child is stricken with measles in a household in which there are other susceptible children it should be promptly isolated. The isolation should not be delayed until the diagnosis is confirmed by the appearance of the eruption, but upon the first suspicion that the disease might be measles.

In selecting an apartment for the patient such a room or, preferably, a suite of rooms is to be chosen as can be most effectually separated from the rest of the house. It will usually be found that the uppermost rooms of the house are most suitable and available. In choosing the apartment care should be given to the facilities for ventilation. Admirable ventilation is furnished by an open fireplace in which fire is kept constantly burning, but such a convenience will usually be found wanting. The most common method of securing the necessary change of air is from a window sufficiently removed from the sick-bed to avoid direct currents of air striking the patient. A rather safer method, particularly in such a disease as measles, is to ventilate through the adjoining room, as suggested by J. P. C. Griffith.¹ The windows of this room may be kept open and the fresh air permitted to enter the sick-room through the communicating door, which is opened for this purpose from time to time. As this room also forms the channel of communication with the remainder of the house, the opening of the windows will tend to dilute or dissipate the infection.

All unnecessary articles of furniture, such as drapery, carpets, and upholstery should be removed. The spaces around doors communicating with parts of the house to be protected should be sealed by pasting strips of wrapping paper over them. The contagium of measles is so diffusible that unless this precaution is taken the infection will travel beyond the sick-chamber. Over the door leading into the corridor should be suspended a sheet which is kept moist with diluted Labarraque's solution, carbolic acid (5 per cent.), or a 1:1000 solution of corrosive sublimate.

The woodwork and the floors of the apartment should be kept clean by mopping with cloths saturated with antiseptic solutions. Owing to the liability to pulmonary complications in measles, sweeping of the sick-room should be assiduously avoided.

The nurse or attendant should not leave the sick-apartments save after change of clothing and thorough ablution. If the mother wait upon her child she should devote her time exclusively to the patient, and not come in contact with susceptible members of the family. Such garments should be worn by the nurse or mother as can be readily washed.

All articles coming in contact with the patient, such as dishes, bed and body linen, etc., should be disinfected in the adjoining room, where solutions for this purpose should be kept on hand. A 5 per cent. solution of carbolic acid will suffice for this purpose, although for the dishes boiling water is to be preferred.

¹ Hare's System of Practical Therapeutics, p. 132.

It is a difficult matter to state just how long measles patients should be isolated. Unlike scarlet fever the disease is most contagious early, and the period of infectiousness is short lived. Most pediatricians are of the opinion that the period of isolation should be in all from two to three weeks. In uncomplicated cases two weeks are probably sufficient if desquamation has ceased. Whether or not the desquamation of measles is infectious is an undetermined problem, with plenty of advocates to champion each side of the question. It is proper to state that certain physicians who have had unusual opportunities of judging, such as Hoff, Peterson, and Comby,¹ deny the infectiousness of the stage of desquamation. The last-named observer says: "We know to-day that measles ceases to be contagious after the eruption." In institutions where so much depends on effective isolation, patients should be separated for the full period.

UTILITY OR FUTILITY OF ISOLATION.—There are many physicians who deem isolation in private residences futile and, therefore, do not advise it. It must be admitted that when measles appears in a child to whom susceptible children have been freely exposed, isolation is too late. If, however, patients are isolated upon the first suspicion of measles, a certain small proportion of the exposed will probably escape, particularly babies, whose susceptibility is slight and whom it is particularly important to protect. Where such young infants can be sent to another household this course is eminently desirable, provided no susceptible children be there resident. It is unjustifiable to send exposed children to a home where unprotected persons reside, for these in turn would be exposed upon the former falling ill.

It is, of course, recognized that the method of isolation above outlined could not be carried out among the poor nor in families living in restricted quarters. Moreover, there are many people who would refuse to go to such inconvenience and expense, with the knowledge that the benefits to be derived are doubtful. We feel that when measles breaks out in a household in which unprotected persons, particularly children under three years of age, live, the proper course to pursue is to isolate the patient. Such a procedure would, in the long run, save lives.

When measles develops in an institution for children, the patient should be immediately isolated. No new admissions should be permitted save to quarters which are completely separated and protected from the infected apartments. The exposed children should be kept under close surveillance until the extreme limits of the period of incubation have been passed.

Desquamation.—The germs of measles have comparatively little tenacity outside of the human body. It is unusual for the disease to be caused by infected articles or third persons. We do not subscribe, however, to the positive statements made by some physicians that the disease is never communicated in this manner. In hospitals and other institutions for children wards should invariably be disinfected after

¹ Loc. cit., p. 200.

measles has broken out; in private households thorough cleansing and subsequent airing may take the place of the more rigid measures of disinfection employed in other infectious diseases.

General Management of the Disease.—Measles runs its course in a definite period of time like other self-limited affections, and tends in uncomplicated cases to recovery. No known drug is able to abridge or modify the course of the disease. The therapeutic indications, therefore, are: (1) to mitigate or control excessively developed symptoms and (2) to treat or, preferably, prevent complications.

The temperature of the sick-room should be maintained in the neighborhood of 70° F., particularly during the cold months of the year. It is important that the temperature be kept uniform and not be allowed to fall during the hours of the night. While it is desirable to avoid direct draughts upon the patient, it is equally essential to keep the room well ventilated and the air pure. Owing to the irritating influence of dry air and the increased liability to dissemination of dust in such an atmosphere, it will be found advantageous to moisten the air by one method or another. A pan of water may be heated over an alcohol lamp or the old-fashioned kettle of steaming water may be brought into the room. This use of steam is even more important when a severe catarrhal laryngitis or bronchitis is present. Under such circumstances aromatic and sedative medicaments, such as the compound tincture of benzoin may be volatilized by being placed upon the surface of the steaming water.

The habit, fortunately obsolete for the most part now, of bundling up measles patients with an excess of bed-clothes is to be deprecated.

Mothers should be instructed that the guide in this matter is the comfort of the patient. Sydenham proved several centuries ago that the "sweating regimen" was out of place with a feverish patient. In changing the bed-linen of patients in the winter months it is advisable to warm the sheets before they come in contact with the patient.

It will be found necessary to protect the eyes of measles patients against too strong rays of light. It should be remembered, however, that it is not necessary to make a room absolutely dark in order to accomplish this purpose. Just sufficient light should be excluded to make the patient comfortable. The complete shutting out of daylight is not only depressing, but the air is robbed of the purifying and germ-destroying influence of the sun's rays.

Patients with measles may be sponged daily with tepid water. The old-time prejudice against the use of water in the eruptive fevers is still harbored by some oversolicitous mothers, but is scouted by physicians of experience.

In order to avoid complications which arise from the catarrhal inflammation of the nose, mouth, and conjunctiva, it is well to employ the following *preventive measures* as a routine. The mouth should be washed several times a day with a solution of boric acid to which a little glycerin and a few drops of oil of wintergreen may be added, or instead some other mild antiseptic wash may be employed. By this

precautionary measure the liability to ulcerative stomatitis, a by no means rare occurrence, is lessened. Williams regards the use of antiseptic mouth washes as important, because "it has been shown that the microbes associated with bronchopneumonia are present in the mouth in more than half the cases of measles."

The nares should be irrigated every few hours with a decinormal saline solution. Care should be taken that the syringe is gently manipulated and the forcible projection of fluid into the nose avoided.

Comby prefers spraying of the nose, mouth, and throat with a steam-atomizer. He states that Siredey obtained excellent results by this method at l'Hôpital d'Aubervilliers; before this treatment was used 50 cases of measles gave 23 complications (46 per cent.); since the employment of the spray 53 cases have only furnished 7 complications (13 per cent.). The genitalia, particularly in girls, should be kept scrupulously clean owing to the vulnerability of these parts to gangrene involvement. In addition to the use of soap and water a weak solution of bichloride of mercury or a saturated solution of boric acid may be employed.

Measles patients should always be *confined to bed* for the entire febrile period of the disease; in severe cases the patient should not be allowed to leave bed until a week or ten days after the termination of fever. During the cold and rainy seasons this precaution should be carefully observed. During the balmy days of late spring or summer one need not adhere so rigidly to this rule. It is difficult to keep very young, restless children constantly in their cribs; where care is exercised as to the equability of the temperature in the room and to the clothing of the child, it is permissible to gratify its desire to be taken up in one's arms. Season and climate will influence the duration of the sojourn in-doors. Ordinarily the patient should not go out for ten days to two weeks after the subsidence of fever; this period should be increased in cold, wintry weather, and abbreviated during a warm and dry spell.

Diet.—For children, milk, preferably diluted with barley-water, is the best diet. This not only constitutes the most assimilable and nourishing food, but helps to assuage the thirst and acts on the kidneys. When the temperature is high the milk may be taken cool and will be found to be most acceptable to the patient. Where it is distasteful to a child it may often be rendered more palatable by flavoring it with a little extract of vanilla. As measles is a disease of short duration it is not essential to force nourishment upon the patients as in more protracted affections, such as typhoid fever.

It will be found that when the temperature is high, children will want nothing but cool milk; later there will be a desire for a more varied dietary. As the fever declines there is no objection to the use of junket, farina, milk-toast, broths, arrowroot, rice, custard, strained oatmeal, soft-boiled eggs. It will be well to avoid those cereals which, by reason of their husk, are apt to excite diarrhoea.

For the relief of thirst, apart from the use of cool milk, the patient may partake freely of water, provided it is not iced. In older children

carbonated water is often gratefully received, or water acidulated with lemon or orange juice.

There is no objection to the use of ice-cream, provided it is taken in moderation.

Medical Treatment in the Complicated Cases.—Mild cases of measles require but little medication; the nursing is of greater importance. It may be necessary to relieve constipation in the beginning. No irritant purgatives should be employed, but rather such gentle remedies as castor oil, elixir of cascara, or syrup of rhubarb, or a simple enema may be given. Drastic drugs might lead to a catarrhal inflammation of the intestines, to which measles patients are already predisposed. More often the physician will be called upon to check excessive bowel movements. If these are allowed to continue they soon exhaust the vitality of the patient. Usually the diarrhoea can be controlled by a mixture containing paregoric and bismuth; if this does not suffice the deodorized tincture of opium may be used instead of paregoric.

Where the bronchial catarrh is slight no treatment is necessary. When there is much cough it will be necessary to allay it by one of the simple cough mixtures. The well-known "brown mixture" may be administered or a combination containing a little bromide of soda and ipecacuanha may be used. For severe and incessant cough one may be obliged to resort to opium; it must be remembered that this drug must be used with caution in young children. Five to twenty drops of paregoric, according to the age of the child, may be given every few hours.

The fever, when of moderate grade (102° F.), will require no treatment. It is customary to prescribe some simple febrifuge containing a little tincture of aconite, potassium citrate, and spirits of nitrous ether; this preparation has a gentle diuretic and diaphoretic action. When the temperature reaches 104° or 105° F., and particularly when it is accompanied by marked nervous symptoms, such as restlessness, delirium, stupor, or convulsions, more active antipyretic treatment is demanded. Of all measures for the reduction of temperature, hydrotherapy is to be preferred. Cold tub baths are usually not well borne by young children, and it is best to employ tepid or warm baths, except where the fever cannot be thus controlled. Immersion in a bath of 85° F. to 90° F. will frequently bring down the temperature and quiet the disturbed nervous system. These baths may be repeated as often as the occasion demands. In those cases in which the temperature is not sufficiently controlled by this means, recourse may be had to the use of cold sponge baths or the use of the wet pack. The ice-cap may be used as an adjunct to any of these measures.

When the temperature is high and the extremities cold, the patient may be immersed in a hot bath with or without the addition of mustard; in such cases the ice-bag should be applied to the head. The cold bath under such circumstances is badly borne, as the depression is too great for an already weak heart.

The hot bath with mustard is also useful in those cases in which the eruption is imperfectly developed or unusually slow in making its appearance.

The reduction in the body temperature is accompanied by an amelioration of the pronounced nervous symptoms which accompany hyperpyrexia. Where for any reason hydrotherapy cannot be employed, one may resort to the use of some of the coal-tar antipyretics. Antipyrin usually acts very well in children. It has been extensively employed by many physicians with satisfactory results. Not only is there a reduction in the temperature, but violent nervous manifestations, when present, are promptly quieted. One to 3 grains repeated according to indications will usually suffice. Comby has used this drug extensively in measles, giving it in dosage of $7\frac{1}{2}$ to 15 grains. We would feel a hesitancy about administering such a dose to a child, yet Comby states that he has never seen any bad results therefrom; a reduction of temperature of one or two degrees was obtained, which lasted from two to four hours. Phenacetin may, if desired, be employed instead of antipyrin. While these drugs usually act well, hydrotherapy is ordinarily to be preferred.

Treatment of Complications.—Measles as an uncomplicated disease nearly always ends in recovery; it is its complications which render it frequently a grave and fatal affection. The preventive measures to be pursued have already been discussed. The complicating disorders must be treated much in the same manner as when they occur independently of measles.

Nervous Symptoms.—The ushering in of an attack of measles with convulsions is not of bad augury unless they persist; convulsions in children take the place of the chill in adults. Where the seizure is brief no special treatment is necessary; when it is prolonged or repeated there is a possibility of a cerebral hemorrhage resulting therefrom and measures should be taken to check the convulsions. A few inhalations of chloroform will frequently control the paroxysm, after which chloral hydrate or antipyrin should be administered. An ice-bag to the head will also be found to be of assistance.

Restlessness, stupor, or delirium can be controlled by the hydrotherapeutic measures mentioned, for they almost always occur in association with high temperature.

Skin.—The skin should be kept scrupulously clean throughout the attack; this may be accomplished by sponge baths with alcohol and water or mild antiseptic solutions.

Itching of the skin may be so intense as to necessitate measures for relief. A lotion containing 1 drachm each of carbolic acid and glycerin to the pint of water or an ointment of 10 grains each of carbolic acid and camphor to the ounce of vaselin will control the pruritus. Not infrequently impetigo vesicles and pustules develop about the nose, mouth, or ears as a result of pyogenic infection of the skin from purulent discharges. An ammoniated mercury ointment, 10 grains to the ounce, will effect the disappearance of these lesions.

Ulcerative Stomatitis.—Ulcerative stomatitis is to be treated by the frequent use of antiseptic mouth washes, such as diluted Dobell's solution or hydrogen peroxide. Where there is much ulcerative action benefit will be derived from painting the ulcers each day with tincture of iodine.

Cancrum Oris.—When that frightful complication *cancrum oris* develops prompt and energetic treatment is demanded. As soon as the condition is discovered the patient should be given a few whiffs of an anæsthetic, the pultaceous mass upon the mucous surface of the cheek curetted away, and the base thoroughly cauterized with fuming nitric acid. If despite this the gangrene should appear upon the cutaneous surface of the cheek, the affected area should be promptly and freely excised. One must not be deterred for fear of the resulting disfigurement, for only the most radical treatment will give a chance for life. The vital powers should be supported by concentrated liquid nourishment and by stimulants.

Coryza.—When coryza is an annoying symptom considerable relief will be afforded by irrigating with saline solution and subsequently spraying the nares with albolene containing 2 grains of menthol to the ounce. This procedure may be repeated every few hours if necessary.

Nose-bleed.—Nose-bleed, when moderate, need not be interfered with, as it lessens the congestion of the nasal structures. When it is severe or persistent it may be checked by the injection of hot water, a solution of antipyrin, or, if necessary, the perchloride of iron. When the hemorrhage is from the anterior portion of the nose the nares may be plugged with sublimated absorbent cotton.

Conjunctivitis.—The conjunctivitis is often sufficiently pronounced to require measures for its relief. The light in the sick-room should be kept subdued. Cool, moist compresses may be applied to the lids and a boric acid eye wash instilled several times a day. Where there is considerable gluing together of the lids by the drying of the conjunctival discharge, the borders of the lids should be anointed with an ointment of $\frac{1}{2}$ grain of the yellow oxide of mercury to the drachm of vaselin.

Laryngitis.—Laryngitis is present in the vast majority of cases. When it is mild the application of moist compresses to the neck will be all that is necessary. These may be applied cold and changed three or four times in the course of twenty-four hours. When the laryngitis is accompanied by spasmodic paroxysms the compresses should be hot. The atmosphere of the room should be kept moist. When symptoms of croup are pronounced it is a good plan to make a tent of the bed-clothing and direct the spout of a croup kettle into the tent. Lime-water may be evaporated instead of ordinary water; the patient should also be encouraged to drink freely of water, particularly alkaline waters. Jacobi recommends the internal administration of the iodide of potassium in moderate doses and also an opiate at night. Dover's powder has long been regarded as a useful remedy in relieving laryngeal spasm.

In laryngeal stenosis, von Jürgensen advises a hypodermic injection of apomorphine hydrochlorate sufficient to induce vomiting. It should be remembered that a persistent stenosis of the larynx after measles

means the presence of a false membrane, and that this may result either from the presence of the streptococcus or the diphtheria bacillus. This serious condition requires prompt and energetic treatment. If *diphtheria* is suspected the usual treatment, including the administration of antitoxin, should be immediately instituted. The prognosis appears to be equally grave whatever be the character of the membranous exudate, for bronchopneumonia is extremely apt to supervene. When the stenosis leads to urgent dyspnoea, intubation becomes necessary. This operation will give temporary relief, but it seldom averts the fatal outcome.

Bronchopneumonia.—Bronchopneumonia is the most frequent and the most fatal of all of the complications of measles. Every effort should be made to prevent the development of this dreaded complication by attention to hygiene and nursing, as already pointed out. The utmost vigilance is necessary to detect the earliest symptoms of this disease. Holt aptly says: "Very little can be done for the disease, but much can be done for the patient." The chest should be enveloped in a jacket of cotton-batting or oiled silk. Counterirritation in the form of mustard-wheat-flour paste may be applied to the chest from time to time. When the temperature is high and the pulse of good volume, ice poultices over the chest accomplish a double purpose.

Children should not be allowed to be continuously in the same position, but should be moved from time to time. Infants may be carried in the nurse's arms. Steam inhalations will be found useful when there is much bronchial secretion; these may be medicated with a little creosote. No antipyretic treatment is necessary unless the temperature rises above 103° F. The coal-tar derivatives should, in general, be avoided, as they are depressant in sufficient dosage. Hydrotherapy should be depended upon to lower the temperature when it is excessive and to allay the accompanying nervous symptoms. For this purpose the graduated bath, the wet pack, sponge bath, or ice-cap can be employed. Friction of the extremities during the bath will help to maintain the peripheral circulation. Brandy may be administered before the bath and heat applied to the feet afterward.

Where there is much cyanosis a warm mustard bath with the ice-cap to the head will be found useful.

The alternate application of hot and cold douches favors deep respiration, a condition eminently to be desired. Jacobi says: "Warm bathing and cold affusion in a warm bath will be of good service, for it is necessary that the patients, particularly small children, should cry. Unless they cry they will suffocate." For the purpose of stimulating deep breathing and expectoration Thomas recommends the use of a folded sheet wrung out of cold water wrapped around the chest; this procedure may be frequently repeated, particularly if the temperature is high.

Emetics and depressant expectorants are to be avoided. Carbonate of ammonia in 1 to 2 grain dosage, every three or four hours, will be found of value. We have found that it is much better borne when administered in milk. Aromatic spirits of ammonia may be given

when the stomach will not bear the carbonate. It is highly important to interrupt the use of any drug that disturbs the stomach.

Whiskey and brandy are of great value, but should be reserved until they are needed; they should not be pushed in the beginning before the heart shows evidence of weakness. When the pulse becomes small and rapid they are to be administered freely; a one-year-old child will bear one to two ounces of whiskey a day. Strychnine is a valuable remedy and may be given in doses of $\frac{1}{300}$ of a grain every three or four hours to a child one year old.

Nitroglycerin or the nitrite of amyl is useful to tide over acute cardiac depression.

When cyanosis makes its appearance oxygen should be resorted to. It may be given for long periods freely mixed with air. A good plan is to introduce the oxygen beneath a bed-tent. Sudden collapse should be combated by the use of oxygen, whiskey, strychnine, and a hot mustard bath.

In treating cases of bronchopneumonia following measles in hospitals it is a wise precaution to isolate these patients from the uncomplicated measles patients. Holt says: "Twice in one institution have I seen regular epidemics of bronchopneumonia occur with outbreaks of measles, in some of the wards nearly every case of measles developing pneumonia."

In the Hôpital des Enfants Malades, at Paris, all cases of bronchopneumonia are treated in isolated compartments in the ward. The partitions are eight feet high and constructed in part of glass; each compartment is open at the top and has a window opening upon the exterior. It was deemed desirable to isolate cases of bronchopneumonia because the disease was considered very infectious and because the severity of the attack appeared to be diminished thereby.¹

Otitis Media.—Otitis media is a common complication of measles. If neglected it may give rise to more serious conditions, such as mastoid or cerebral abscess.

By the assiduous use of mild antiseptic solutions in the nose and throat in measles much may be done to prevent extension of inflammation to the middle ear.

The Eustachian tube of very young children is relatively of large size, and pyogenic germs in the nasopharynx can find ready access to the middle ear. The key-note of prophylaxis, therefore, is cleanliness. The nasopharynx should be sprayed with warm, bland liquids, such as boric acid or decinormal saline solution, after which a weak mentholated liquid vaselin should be introduced. Children should be encouraged to blow the nose frequently to dislodge the adherent mucus. In very young children, and especially when adenoid vegetations are present, Downie² advises gentle inflation of the nostrils by means of the Pollitzer bag. This manipulation should not be entrusted to a nurse, but should be performed by the physician himself. The child is instructed to forcibly

¹ Quoted by Dawson Williams, loc. cit.

² Quoted by Williams.

breathe out through the mouth at the moment the air is inflated through the nose. In this manner the mucopurulent discharge is forced into the mouth from the nasopharynx.

When otitis develops and the pain is severe, measures must be employed for its relief. Heat should be applied to the external ear; dry heat is to be preferred to moist applications. A hot salt, bran, or water bag may be placed over the ear, with a towel interposed. A few drops of a 3 per cent. solution of cocaine instilled into the ear often gives relief; oily solutions for this purpose are to be avoided. Tincture of iodine may be painted over the mastoid region. It will be necessary in some cases to give an opiate, preferably in the form of paregoric, to relieve the pain and induce sleep.

The persistence of the pain with an increase in temperature indicates the performance of a paracentesis tympani.

Incision should be made in the posterior inferior segment. Relief is often immediate, although pus may not be discharged until later. It is a good plan to expel the pus after puncture by inflation of the nose with the Pollitzer bag. The auditory meatus should then be cleansed with a warm saturated solution of boric acid or a 1:5000 solution of corrosive sublimate. The patient should be encouraged to lie upon the affected side to favor evacuation. The use of absorbent cotton in the ear should be avoided.

The *urine* should be examined from time to time to exclude the presence of kidney involvement. Nephritis is relatively rare in measles, but it has been discovered often enough to justify some care in this direction.

During *convalescence* children should be restrained from the excessive use of the eyes, which are still in a weak condition. The persistence of cough, particularly with slight evening rises of temperature, should put one on guard against the possible development of tuberculosis. Children thus affected should, if possible, be taken to a locality where the climate is warm, dry, and equable. Creosote and cod-liver oil will be found to be among the most useful remedies for this persistent cough.

CHAPTER X.

RUBELLA.

Definition.—Rubella is an acute, contagious, epidemic disease, characterized by an eruption of barely elevated, rose-colored macules, slight catarrhal symptoms, and mild febrile disturbance, running a course lasting usually three or four days. Rubella is a specific entity, unrelated to either measles or scarlet fever, and protecting only against future attacks of the same affection.

Synonyms.—*German measles; Rötheln.* There is an embarrassment of riches in the various designations applied to this disease. The Germans use the terms *rötheln* and *rubeola*; the French call it *rubeole*. The latter term being used at times to denote true measles, it is confusing to apply it to another disease. Among other appellations are *rubeola sine catarrho* or *incocta*, *rubeola notha*, *rubeola epidemica*, *rubeola morbillosa*, *rubeola scarlatinosa*, *rosania*, *roseola*, *roseola epidemica*, *rosalia*, *exanthème fugace*, *essera Vogelii*; *hybrid*, *bastard*, *spurious*, or *imperfect measles*; *hybrid* or *bastard scarlatina*, *rougeole fausse*, *feuer masern*, *German measles*, *French measles*, etc. The last-named terms should not be employed, for rubella is a disease entirely distinct from measles, although often strongly resembling it. Griffith counsels the adoption of the latin term *rubella*, which was introduced by Veale in 1866 and accepted by Squire and others.

History.—The vagueness of the very early medical writings and the use of confusing names make it difficult to establish the origin of the exanthematous diseases with any degree of accuracy. It is possible that the Arabian physician Avicenna (A.D. 980 to 1037) observed rubella, for he refers under the name of *Hhamikah* to a disease related to measles.

In the seventeenth century Ingrassias, Ballonicus, and Sennertus noted an eruptive disease similar to measles, and it is believed by some writers that this was rubella.

The first accurate and undoubted references to the disease were published in the middle of the eighteenth century by the German physicians de Bergen (1752) and Orlow (1758). These served to define the nosological position of rubella (then called *roseolâ*) and to distinguish it from both measles and scarlatina. But some of the writers in the next half-century evidently confused the disease with scarlatina and other affections, for neither the descriptions nor the mortality rate conform with that of rubella. Selle in 1780 and Formey in 1796 report virulent and fatal epidemics. Formey states that between 1784 and 1796 there died of the disease in Berlin 1180 persons, while there

were but 203 deaths from scarlet fever and 103 deaths from measles.¹ While the specific nature of the disease was maintained by Ziegler (1788), Fielitz (1796), Sprengel and Stark, it was denied by many later writers.² Both Gode in 1822 and Jahn in 1835 were skeptical concerning rubella, the former regarding it as a form of scarlatina and the latter denying its existence altogether. Hufeland, Frank, and Reil looked upon rubella as a modified scarlatina, as did likewise the renowned Heim, who thought it was more to be dreaded than the ordinary form of scarlet fever. The confusion increased. Naumann rejected the specific nature of the disease and classified his cases partly as measles and partly as scarlatina.

Hildebrand in 1825 and Schönlein in 1832 regarded rubella as the hermaphroditic offspring of scarlatina and measles. They assumed that the poisons of scarlet fever and measles combined to produce the disease, and that, therefore, rubella was a hybrid between these two affections. This view was accepted by many writers, including Geertsema (1821), Busche (1841), Paasch (1854), and Gelmo (1858).

The great Viennese dermatologist Hebra repudiated the specificity of rubella, as did likewise Canstatt and Gintrac. But the truth concerning this third disease could not long be submerged. Behrend (1828) and Wagner (1834) had previously insisted on the distinctive nature of rubella, and the weight of the celebrated Trousseau's opinion was to be added to theirs. After 1860, numerous champions arose to defend the new creed, among whom were Thierfelder, de Man, Henning, Dnais, Mettenheimer, Veale, Lindwurm, Arnold, Vogel, Wunderlich, Dunlop, Squire, Gerhardt, Emminghaus, Küster, and finally Thomas, from whom this list is quoted.

In England, as in Germany, belief in the existence of this disease alternated with periods of skepticism. Willan (1808) observed an exanthematic disorder allied to measles, but without prodromal catarrhal symptoms. He regarded it as a species of measles, but significantly remarked that "persons receiving the miasm in this form are peculiarly liable to a second attack of measles." In 1840 Patterson advocated the specific character of rubella, and Tripe in 1852 and Balfour in 1854 expressed similar opinions. In 1866 Veale suggested the name rubella for the disease; Murchison (1870), Dunlop (1871), and Liveing (1874) all endorsed its specific nature. Within more recent years epidemics in England³ have been reported by Cheadle (30 cases), Shuttleworth, Douglass (50 cases), Tongue-Smith (145 cases), Wilson, Dukes (63 cases), and McLeod in Calcutta.

Homans, of Boston, in 1843 was the first physician in this country to call attention to the disease. Cotting published papers on the subject in 1853 and 1871. Howard in 1871 and J. Lewis Smith in 1874 also

¹ Thomas gives the figures a little differently. Deaths from rubella from 1784 to 1794, 457; from scarlet fever, 172; from measles, 53.

² For much of the history and bibliography of rubella, as well as for other information, we are indebted to the admirable and exhaustive paper of J. P. Croser Griffith, *Medical Record*, July 2, 1897.

³ Mentioned by Griffith, *loc. cit.*

directed the attention of American physicians to the existence of rubella. The chief epidemics reported in this country have been by Hatfield (110 cases), Park (over 100 cases), Earle (120 cases), Edwards (166 cases), Kingsley (21 cases), Atkinson, Griffith, and Hardaway.

At the present day there is a unanimity of opinion concerning the existence of rubella as a disease *sui generis*.

THE ETIOLOGY OF RUBELLA.

It is generally recognized that rubella, like the other exanthematous diseases, is derived from and begets a like disorder. It confers protection only against rubella, and no immunity against it is granted by an attack of measles or scarlet fever.

Many of the earlier writers doubted and even denied the contagiousness of rubella, but there is at the present day a unanimity of opinion concerning its transmissibility. As to the *degree of contagiousness* views are somewhat divergent. Chadbourne and J. Lewis Smith regarded it as feebly contagious; Thomas, Liveing, Tongue-Smith, Bourneville, and others, as less contagious than measles; Jacobi, Dukes, Squire, and Griffith look upon it as very contagious, and Edwards¹ believes that "rubella is one of the most contagious of all of the eruptive fevers." Griffith states that in an institution of 100 children 37 took the disease despite prompt and careful isolation. In another institution 26 per cent. were attacked. Klaatsch believes that the degree of contagiousness varies in different epidemics.

Hatfield² reports an asylum epidemic in which 110 inmates out of 196 contracted the disease.

From our experience at the Municipal Hospital we are inclined to believe that a larger number of children escape rubella when this infection is introduced into the wards than escape measles under similar circumstances.

Rubella is essentially an *epidemic* disease and appears to be more prevalent in the winter and spring seasons. The disease is about as common as measles, with which affection it has doubtless often been confounded. The infection of rubella seems to be more tenacious and persistent than that of measles. It is, therefore, more apt to be carried by *fomites* in the garments of third persons than is measles. Edwards alleges that about 75 per cent. of his cases could be directly traced to infection from the bunks of ships, and states that Emminghaus, Thomas, Veale, and others considered such an origin proved. Corlett³ remarks that rubella corresponds more with scarlet fever than with measles in the persistence of the vitality of the contagium.

Opinions are at some variance in regard to the period of greatest contagiousness. Thierfelder looked upon the stage of convalescence as the time at which the disease was most transmissible. Squire considered all stages contagious, from the pre-eruptive period late into

¹ Article on Rubella, Keating's Cyclopaedia of Diseases of Children, Philadelphia, 1889, p. 687.

² Chicago Medical Examiner, August, 1881.

³ Loc. cit.

convalescence. Edwards coincides with this opinion. Griffith concludes, from his observation in institution epidemics, that rubella is certainly contagious at a very early date, for prompt isolation failed to check the extension of the disease.

Age.—Rubella behaves much like measles as regards age incidence. Infants under six months of age usually escape the infection, although now and then the disease will be contracted. We have seen a six-month-old infant live and remain well for months in a ward in which cases of rubella were constantly appearing. Smith, Roth, Steiner, and Hardaway have recorded attacks in early infancy, and Scholl reports a case occurring in a child a few days after birth, the mother having suffered from the disease two months previously. As in measles, those who escape the disease in childhood may contract it in adult life; indeed, even in advanced years, as is attested by Seitz, who reports a case in a woman seventy-three years old.

Emminghaus saw only two adult attacks among 42 cases. Thomas noted 3 among 77 cases; Kassowitz observed 5 in 64 cases and Thomas but 1 in 100 cases. Edwards does not believe that adult life confers any special immunity; he regards infrequent exposures to the disease, and protection by an attack in childhood as the cause of the comparative rarity among adults.

Thomas holds a rather different view. He says: "After the fortieth year the susceptibility is nearly lost, and we may consider it as essentially weakened at puberty, and as steadily diminishing subsequently." In Forchheimer's¹ experience more physicians have been attacked by rubella than by all the other exanthematous diseases taken together. He adds that, "with the exception of variola, possibly no disease of this class so frequently affects adults."

THE SYMPTOMATOLOGY OF RUBELLA.

Period of Incubation.—Different observers have assigned incubative periods to rubella varying from five days to three weeks. This variable duration is regarded by Griffith as one of the diagnostic features of the disease and in striking contrast with the fixed incubation period of measles. To indicate the divergent observations of different clinicians we present a table compiled by Forchheimer, to which we have made additions:

¹ Twentieth Century Practice of Medicine, article on Rubella, p. 180.

PERIODS OF INCUBATION OF RUBELLA.

Atkinson . . .	14 to 21 days.	Hardaway . . .	2 weeks or longer.
Balfour . . .	2 weeks.	Hatfield . . .	10 days.
Boudet . . .	12 to 14 days.	Jacobi . . .	14 to 21 days.
Bourneville . . .	8 days.	Kassowitz . . .	2 to 3 weeks.
Bricon . . .	8 to 10 days.	Klaatsch . . .	2½ to 3 weeks.
Bristowe . . .	1 week.	Longstet . . .	18 days.
Cheadle . . .	15 days.	Mettenheimer . . .	2 weeks or longer.
Clausen . . .	17 to 20 days.	Musser . . .	Just 6 days in 1 case.
Cotting . . .	3 weeks.	Picot . . .	2 to 3 weeks.
Cullingworth . . .	2 weeks.	Pollock . . .	6 to 16 days.
Cuomo . . .	17 days; never less.	Juhel-Renoy . . .	15 days.
Duckworth . . .	16 days.	Robinson . . .	6 to 7 days.
Duke . . .	15 to 16 days.	Scholl . . .	5 to 21 days.
Earle . . .	17 to 21 days.	Steiner . . .	10 to 14 days.
Edwards . . .	10 to 12 days.	J. L. Smith . . .	7 to 21 days.
Eichhorst . . .	2 to 3 weeks.	Tongue-Smith . . .	14 days.
Emminghaus . . .	2 to 3 weeks.	Squire . . .	8 to 21 days.
Gerhardt . . .	2 to 3 weeks.	Thierfelder . . .	2 weeks or longer.
Glaister . . .	4 to 5 days or longer.	Thomas . . .	2½ to 3 weeks.
Goodhart . . .	2 weeks or longer.	Vacher . . .	13 days.
Griffith . . .	5 to 11 days.		

It is thus seen that the incubation may be either shorter or longer than that of measles. Eleven writers have noted minimum periods of five to eight days, and no less than thirty-two have seen the period extend beyond fourteen days.

During the stage of incubation the patient is entirely free of any disturbance of health except, perhaps, in extremely exceptional cases.

Period of Invasion.—In most cases of rubella this stage is either devoid of symptoms or presents only mild manifestations which are readily overlooked. It would appear that the more severe the attack is to be, the more apt is it to be preceded by pronounced prodromal symptoms. In the vast majority of our cases at the hospital the eruption was the first sign to attract attention. In a severe attack in a trained nurse, the symptoms of which will be fully detailed later, there was, however, a distinct and protracted stage of invasion. This nurse was on night duty in a ward in which rubella existed. On Wednesday, March 11, 1903, she was taken ill with headache and sudden vomiting; the emesis was persistent, the patient vomiting four or five times each day and retaining nothing. There were also feverishness, continued headache, recurring chilliness, perspiration during sleep, restlessness, and weakness. On March 16th, *four and a half days later*, the eruption appeared. No catarrhal symptoms whatever were present. This case must be regarded as presenting exceptional initial manifestations.

While most writers refer to very mild and brief prodromes, some rather severe invasive symptoms have been described. Edwards¹ noted in a severe epidemic in the Philadelphia Hospital the following symptoms: chilliness, languor, faintness, headache (more or less severe), pain in the back and limbs, coryza, red and watery eyes, sore throat, cough, occasionally a hoarse, husky voice, and a temperature from

¹ Loc. cit.

100° to 103° F.; nausea and vomiting, delirium and convulsions, and epistaxis were observed in three cases.

Other unusual prodromal symptoms have been recorded. Prioleau reports 2 cases of hemorrhage from the eyes and ears; vomiting is mentioned as a rare symptom by Smith, Murchison, McLeod, and Emminghaus; convulsions by Smith, Lindwurm, Cuomo, and Alexander; delirium by Hardaway and Cuomo. Nymann observed rigor in 19 out of 119 cases; Earle, Kingsley, Thierfelder and Griffith mention a slight redness preceding the eruption, and Cuomo (in 7 cases) and Edwards (in 4 cases) a prodromal erythema.

Such symptoms as those detailed are exceptional, but nevertheless of interest. The experience of most observers is that the prodromal symptoms are absent or mild, consisting of drowsiness, anorexia, "liquidy" eyes, sneezing, slight cough, etc.

Earle found that prodromal symptoms were more frequently present in adults than in children.

As to the duration of the invasive period, opinions differ somewhat; we would subscribe to the statement of Thomas, endorsed by Hardaway and Griffith, that in the vast majority of cases the prodromal stage is at most no longer than half a day. At the same time we recognize that it may vary from a couple of hours to five days. Various writers assign periods intermediate between these two extremes. It would seem that long periods of invasion presage attacks of greater severity than brief periods.

Period of Eruption.—A half-day or so after the onset of mild invasive symptoms, or in many cases without any prodroma at all, the eruption of rubella makes its appearance. The rash is commonly the first symptom to attract attention, the other mild initiatory disturbances then being recalled. Not infrequently a child awakens in the morning with the eruption visible upon the face. In our cases at the Municipal Hospital, all of which developed in scarlet-fever convalescents, the rash was frequently discovered when the children were lined up for inspection during our visits.

Most writers coincide in the view that the eruption appears first on the face; other locations are, however, mentioned by some observers as the initial site. Liveing and Morris state that it appears first on the trunk; Murchison, Day, and Balfour speak of the breast and arms as first attacked, Willcocks and Carpenter the face and margin of the hair, and Thomas and Corlett the face and scalp. Patterson and Copland assert that it comes out simultaneously on different parts of the body.

In noting the eruption a short time after its appearance upon the face we have seldom failed to find it to some extent on the trunk and arms.

In a severe case in a trained nurse (to which reference has already been made) the eruption was carefully looked for by another nurse occupying the same room and was observed to first appear at 3 A.M. on the legs below the knees: it then spread upward and by 6 A.M. was noticed on the wrists. At 3 P.M., the hour of our examination, it was

PLATE LII.



Eruption of Rubella, showing Discrete but Closely
Set Macules.

present on the legs, arms, and trunk. The face was flushed, but no distinct eruption was seen in this region until the following day.

It is evident that while the eruption of rubella normally appears first on the face, thence extending downward, anomalous cases may occur in which the origin is in other regions.

The exanthem spreads quite rapidly over the body in the course of twenty-four to forty-eight hours. It is interesting to note, however, that the maximum intensity of the rash is not simultaneously noted on the entire cutaneous surface. It is not unusual for the face, chest, and

FIG. 89



Faint eruption of rubella upon the face in a mild attack.

arms to show the eruption at its height while the legs are yet unaffected. When the lower extremities exhibit the exanthem in its greatest intensity it is fading upon the face and upper part of the body. In other words, the rash often seems to pass over the cutaneous surface in a sort of *wave-like progression*. The duration of the eruption at its height in any given region is from a few hours to half a day. The more severe the attack, the longer is the period of maximum intensity and the longer the duration of the eruption.

This peculiar progression of the eruption is commented upon by Thomas in the following words: "It happens with tolerable frequency

that the maxima of its development occur at varying times upon different portions of the body." Some writers, particularly Emminghaus, Roth, Mettenheimer, and Hardaway, attach to this eruptive sequence great importance, regarding it as one of the safest diagnostic signs of rubella. Griffith agrees with Thomas' statement as to the tolerable frequency of this occurrence, but questions its diagnostic value, as he has nearly as often observed that the rash persisted with equal intensity on the face while it spread to the rest of the body, reaching its acme everywhere upon the second day.

Character of the Eruption.—The eruption, in its most typical form, consists of pinhead to lentil-seed sized, pale rose-tinted, slightly elevated, moderately defined macules. The lesions are usually rounded or oval, but may be irregular. The elevation is scarcely sufficient to warrant the use of the term papules, but is appreciable to the finger passed over the surface of the skin. The macules are ordinarily discrete, with considerable intervening pale skin, particularly at the onset of the eruption and on the trunk. Later they are apt to become more closely set and may coalesce, with the production of irregular patches resembling measles or sheets of eruption of a scarlatiniform character.

Ordinarily, macular grouping, such as is seen in measles, is absent, but we have now and then seen distinct linear and crescentic configuration indistinguishable from that observed in measles. Rubella in its purest form, however, shows smaller, more regular, and more discrete lesions than those of measles, which are inclined to present an irregular, blotchy appearance. The color of the macules of rubella has been described as a pale rose-tint or rosy-red by most writers. Shuttleworth refers to it as a brownish-red. The color doubtless varies to some extent in different individuals, as does the tint in all eruptive diseases, but it may be said in general that it is ordinarily not as vivid as the eruption of scarlet fever, nor as dusky or bluish as the measles exanthem.

The discreteness of the slightly elevated macules gives the eruption its distinctive appearance, the reddish spots standing out in striking contrast with the pale integument. Confluence is, however, frequently noted in certain areas, particularly on the face. On the second or third day of the eruption it is not uncommon for the rash to become paler in tint and to assume a more diffuse appearance.

Pressure or irritation of the skin seems to increase the intensity of the eruption and to encourage confluence. Klaatsch and Griffith both report cases in which the eruption was particularly well developed in circular bands above the knees, where the garters had made pressure. In scarlet fever, on the other hand, pressure, such as is produced by garters, is apt to produce anæmic or pale bands in the areas thus affected.

Distribution of the Eruption.—The face almost invariably exhibits an abundance of eruption, especially upon the forehead, cheeks, and chin. The lesions may be so copious as to produce the appearance of slight œdema. The eruption does not respect the circumoral region as does the exanthem of scarlet fever. The scalp is profusely covered, as is also the neck. The chest, abdomen, back, and arms show rather

PLATE LIII.



Rubella exhibiting a Fine Macular Eruption on the
Second Day.

less eruption; the buttocks and posterior aspect of the thighs, owing, perhaps, to pressure, commonly exhibit eruption in such profusion as to present confluent patches. The legs, as a rule, are the seat of the least eruption, the lesions often being widely scattered. It has been asserted by some writers that the palmar and plantar surfaces are exempted, but this is not true, as lesions are not infrequently found in these regions in well-pronounced attacks. The above outline presents the distribution of the eruption in normal cases; it is not rare for departures from this to take place.

Barthez and Rilliet have noted the fading of the eruption followed by the reappearance of the same upon the same day or later. Griffith also mentions a case in which it was invisible during one day and returned.

Duration of the Rash.—The duration of the rash is influenced by the intensity of the eruption and the character of the epidemic. The various periods assigned by different writers are here tabulated:

Altken	4 to 5 days (bad cases 6 to 10).	Gerhardt	$\frac{1}{2}$ to 1 day.
Alexander	14 days (one case).	Griffith	2 to 3 days.
Alibert	2 to 3 days.	Hatfield	4 days.
Balfour	4 to 6 days.	Kingsley	2 to 4 days.
Barthez	2 to 3 days.	Klaatsch	1 to 5 days.
Bourneville	2 to 3 days.	Living	5 to 7 days.
Bricon	2 to 3 days.	Maton	3 to 4 days.
Carpenter	1 to 4 days.	Nymann	2 to 4 days.
Claussen	3 days.	Picot	3 to 4 days.
Copland	4 to 5 days.	Rilliet	2 to 3 days.
Corlett	2 to 4 days.	J. G. Smith	3 days.
Edwards	2 to 15 days; average 5.	Thomas	2 to 3 days.
Emminghaus	2 to 4 days.	Trousseau	1 to 2 days.
Forchheimer	not exceeding 5 days.	Willcocks	1 to 4 days.

It will be seen from the above figures that the duration of the eruption offers considerable latitude. The long periods are doubtless isolated instances. In about 100 cases which we have recently had the opportunity of observing, the rash did not persist beyond three days save in the case of the nurse, in whom it lasted five days. In a great many of the children the eruption was scarcely apparent after the first twenty-four hours; the average duration was certainly not more than two days. The brief duration is, perhaps, to be accounted for by the very mild type of the epidemic. The average duration in over 200 of Edwards' cases was five days; the type of the epidemic which he observed was, however, distinctly more severe than ours.

The rash appears to persist longer in some regions than in others, possibly the regions of greatest intensity. Edwards says that the face and upper chest exhibit the most persistent eruption; our experience coincides more with that of Griffith, who regards the face and buttocks as the seats of the most protracted eruption.

Anomalous Features of the Eruption.—In rare instances miliary vesicles have been noted upon the reddish macules. This has been observed by Curtman, Cuomo, Thomas, Hardaway, and Copland.¹

¹ Mentioned by Griffith, loc. cit.

Petechial spots have been recorded by Dunlop and likewise by Cheadle; Erskine reports similar lesions on the uvula and soft palate. A purpuric rash was also observed by Glaister.

Claussen makes mention of lesions which gave the impression of small shot being buried in the skin. Griffith saw an unusual eruption which also imparted a shotty feel to the finger.

Scarlatiniform Variety of Rubella.—Thus far reference has only been made to normal rubella and to the form which bears more or less of a resemblance to measles. There are other cases in which the exanthem bears a strong resemblance to that of scarlet fever. Some writers of prominence make no mention of this variety and express astonishment at any suggestion of similarity between the rashes of rubella and scarlatina. Thomas says: "According to my observations the exanthem of rubeola (rubella) possesses a similarity to that of measles only, not the slightest to that of a normal scarlet fever." Bristowe and Bourneville and Bricon entertain similar views. These opinions may be attributed to the fact that the scarlatiniform variety of rubella has not come within the range of the personal experience of these physicians.

Mention could be made of a large number of writers who have observed this variety. Hatfield speaks of an epidemic in which the rash in many cases was indistinguishable from measles, and in other cases strongly resembled scarlet fever. J. L. Smith refers to a case which, had he been guided alone by the eruption, he would have regarded as a mild scarlet fever. Griffith describes a case in which the eruption was at first macular, yet on the second day it so closely resembled scarlet fever that he was unable for several days to make a diagnosis. The whole body was covered by a general scarlatinal blush and nowhere could a single macule or papule be found. A short time afterward the brother took rubella.

We have seen in the Municipal Hospital one or two cases of rubella with scarlatiniform eruptions in children convalescent from scarlet fever.

Griffith,¹ from a careful study of a large number of cases, comes to the conclusion that there are two easily recognized types of variation from the character of the eruption in a normal case:

1. "An eruption in which the spots are for the most part nearly or fully the size of a split pea, more or less grouped, and, in fact, having the greatest resemblance to measles.

2. "A rash which is confluent in patches or universally not elevated, and which produces a uniform redness closely simulating that of scarlatina. Very careful examination will often reveal a few papules amid the general diffuse redness."

Desquamation.—Upon the subsidence of the eruption a delicate brownish or yellowish staining may be noticed for a short time.

A slight branny or furfuraceous desquamation occasionally follows the disappearance of the rash. The development of this scaling is proportionate to the severity of the attack and the intensity of the

¹ Loc. cit., p. 15.

PLATE LIV.



Hubella in a Man, aged twenty-one years, with the Scarletinaoid
Type of the Exanthem

eruption. Many writers, including Steiner, Thomas, Fleischmann, Brodie, McLeod, Wilson, Goodhart, Cuomo, Bourneville, and Bricon have not observed desquamation. Edwards, on the other hand, in a severe epidemic discovered desquamation in all of his cases. In quite a number the scaling was well marked; in others it was limited to certain regions, especially the nose. The buccal cavity, particularly the throat proper, participated in the desquamative process. The peeling was usually furfuraceous, beginning in the centre of the eruptive patch and extending to the circumference. Larger scales were seen on the hands and feet. The average duration of desquamation was three days, but Edwards has seen it last twenty days. In our cases, which it will be remembered were very mild, it was rare to see any desquamation.

Associated Symptoms of the Eruptive Stage. Fever.—The extent of febrile reaction in rubella is largely dependent upon the severity of the individual attack and the character of the prevailing epidemic. The variant observations of different writers on this point is evidence of the truth of the above assertion. There are some epidemics in which there is but an insignificant rise of temperature, if, indeed, there be any fever at all. Nymann failed to observe any appreciable rise of temperature in 58 out of 119 cases. Emminghaus, Thomas, Vogel, Wunderlich, Earle, Picot, and others have all seen afebrile cases.

On the other hand, in severe cases high fever may be present. Edwards saw cases with temperature of 103° and 104° F. McLeod's cases ranged from 100° to 105° F. Cheadle reports an epidemic in which the initial temperature was 103° F., later reaching 104° and 105° F. Haig-Brown records a temperature of 105° F., and Davis saw a temperature of 106° F. in a boy with a livid rash, convulsions, and rapidly running pulse.

The fever is, as a rule, proportionate to the extent and severity of the eruptive and catarrhal symptoms.

There is no febrile course which occurs with any degree of constancy. The evening temperature is, however, usually 1 or 2 degrees above the morning. Most cases of rubella will exhibit slight fever varying between 99° and 101° F. In most of our cases the temperature registered 99° or 100° F. In two patients it reached 102° F.

It is not surprising that some of the older writers should have regarded rubella as a hybrid of measles and scarlatina, for we commonly note in this disease the catarrhal symptoms of the former and the angina of the latter, but both in very mild form.

The catarrhal symptoms commonly affect the eyes, nose, throat, and bronchial tubes. The *eyes* are commonly seen to be "watery" or slightly injected. Our experience coincides with that of Griffith, who observed this symptom in about one-half of his cases. It is uncommon to find conjunctivitis and photophobia as pronounced as it is seen in measles.

Sneezing.—Sneezing is a frequent symptom, although the paroxysms may be but few and limited to the first day of the eruption. In none

of our cases did we note any distinct discharge from the nose; nevertheless, *coryza* is recorded as occurring in a considerable proportion of cases in some epidemics.

Cough.—Cough occurs in a variable proportion of cases, depending upon the character of the prevailing epidemic. When it is present it is usually slight and in no sense comparable with the severe cough of measles. It was absent in the vast majority of our cases. Griffith says a loose, bronchial cough was frequently present in his cases and occasionally demanded treatment. In the severe epidemic observed by Edwards cough was generally present, increasing in frequency and severity and occasionally becoming laryngeal. In quite a large proportion of these cases bronchitic rales, more or less diffused, were heard. The cough lasted about as long as the eruption, so that it had entirely disappeared about the fourth or fifth day.

Sore Throat.—Sore throat of a mild character is an extremely common symptom of rubella. The angina is much milder than that observed in scarlatina, and often does not lead to complaint on the part of the patient. Without inspection it would, doubtless, be frequently overlooked. The congestion is most pronounced upon the upper portions of the anterior pillars. Occasionally a more serious involvement of the throat is encountered, characterized by enlargement of the tonsils, swelling of the pharyngeal mucous membrane, and painful swallowing. Mild angina is regarded as a rather constant symptom by most writers.

We have frequently seen upon the *soft palate* a number of pinhead-sized, glistening, reddish elevations. Similar reddish spots have been observed by Emminghaus, Nymann, Gerhardt, Picot, Parke, Dunlap, Kassowitz, Cuomo, and Griffith. Forchheimer regards as a characteristic exanthem "the small, discrete, dark-red, but not dusky papules" which are seen early on the soft palate and which disappear in twelve to fourteen hours.

We have carefully examined the *buccal mucous membrane* in a number of cases and have frequently noted the presence of discrete, pinhead-sized, deep-red spots, bearing a considerable resemblance to the macules upon the cutaneous surface. We have never seen the central bluish-white dots which Koplik describes as characteristic of measles.

Hoarseness.—Hoarseness, usually mild but occasionally severe, has been mentioned by Thomas, Emminghaus, Griffith, Aitken, Cheadle, Patterson, Edwards, and others. The catarrhal symptoms sometimes subside after a duration of a day or two, but more commonly disappear with the eruption. Occasionally a certain amount of cough may continue for some days.

Tongue.—The tongue is usually covered with a thin, grayish coating, the tip occasionally exhibiting some prominence of the papillæ. While a few writers (Balfour, Hemming, Tripe, Murchison, Burnie, and Tompkins) claim to have seen the typical "strawberry" tongue in rubella, this condition must be regarded as exceptional. In some cases the tongue is clean and presents no deviation from the normal appear-

PLATE LV.



Rubella exhibiting an Eruption quite Indistinguishable from Measles.

ance. In severe cases Edwards states that the tongue may be dry and brown.

Lymphatic Glands.—Enlargement of the lymphatic glands has long been regarded as a symptom of considerable diagnostic importance. Nearly all writers are agreed as to the constancy of this adenopathy. It must be remembered, however, that a general glandular intumescence occurs in scarlet fever and to a lesser extent in measles, and that lymphatic enlargement, therefore, does not specially differentiate rubella from these diseases.

According to Griffith, J. F. Meigs regards the enlarged postauricular gland as one of the most prominent diagnostic signs of rubella.

It is claimed by some writers (Squire, Thierfelder, Glover, Jalland, Strover, Hardaway) that the glands increase in size often before the appearance of the rash. In other cases, however, the glandular tumefaction may not be noted until the second day after the appearance of the eruption. The glands behind the ears and those lying posterior to the sternocleidomastoid muscles are those most frequently enlarged, although other glands, such as the inguinal and axillary, may participate in the process. Kassowitz found lymphatic enlargement in but one-third of his cases, and Eustace Smith observed it only in certain epidemics.

Nausea.—Nausea and vomiting are rare symptoms in cases of the average type. In severe cases, however, emesis may be severe and persistent. In one of our cases the vomiting continued for several days before the appearance of the eruption, the patient being unable to retain any nourishment at all. Edwards states that in a severe epidemic in the Philadelphia Hospital, vomiting occurred in a fair proportion of the cases as the eruption was approaching the maximum. In five of these cases it was almost uncontrollable. Griffith observed vomiting on the first day of the eruption in a few severe cases.

The bowels are usually normal or constipated. In a nurse under our care, suffering from a very mild attack of rubella, *diarrhœa* was present on the first and second days of the eruption.

About 40 per cent. of Edwards' cases had gastrointestinal irritation; this very unusual complication may be accounted for by the severity of the epidemic. Among these cases were 10 of enteritis and 2 of enterocolitis. Cuomo has also noted the presence of *diarrhœa* in severe cases. Earle encountered 4 cases of intestinal irritation. Balfour found catarrh of the colon a rather common symptom. The majority of writers make no mention of any disturbance of the bowels.

Itching.—Itching varies both as to frequency and intensity, depending much upon individual peculiarity. It is present in only a minority of cases and is seldom severe.

Pulse and Respiration.—The pulse and respiration usually keep pace with the elevation of temperature. The former may undergo acceleration to 140 or 150 per minute. Edwards says several of his cases presented well-marked symptoms of heart-failure, which yielded, however, to appropriate treatment.

The following case of rubella in an adult patient under our care presents many points of interest:

Miss R., trained nurse, aged twenty-seven years, had measles at the age of eight and scarlatina at the age of six. Was on night duty in convalescent scarlet-fever ward of the Municipal Hospital, in which rubella appeared on March 3, 1903. Patient had been exposed to measles in another building five weeks previously.

March 16, 1903.—On Wednesday, March 11th, the patient was taken sick with headache and sudden vomiting. Since that time she has vomited each day (or rather night, as the patient has continued on night duty, not making known her illness.) Emesis occurred five or six times each night. Patient claims to have retained absolutely nothing. There has also been persistent headache, weakness, recurring chilliness, perspiration during sleep, and restlessness. No catarrhal symptoms whatsoever; neither coryza, cough, nor conjunctival redness.

Although patient had felt feverish for some days, her temperature was first taken on March 15, 1903, in the evening, when it registered 102° F. This morning it is 100° F. Glands about the jaw and neck are not enlarged.

The eruption was carefully watched for by another nurse who occupied the same bed-room; it was observed at 3 A.M. on March 16, 1903, making its appearance first on the legs below the knees, then spreading upward. At 6 A.M. the rash was noticed on the wrists. At 3 P.M. (the hour of our examination) the following notes were made: An eruption of pinhead to lentil-seed sized, dusky red, slightly elevated macules is seen, quite covering the legs and with even greater profusion the arms. The macules form typical *crescents* on the arms and are also arranged linearly. In other places they run together and present an appearance quite indistinguishable from an intense measles exanthem. The upper part of the chest shows a diffuse scarlatiniform redness. On the back are a number of discrete macules which have just appeared. The face shows no distinct eruption, but the cheeks are quite flushed. The buccal mucous membrane exhibits faint reddish spots.

17th. The temperature last night was 101½° F. This A.M. it is 100° F. The patient is perspiring quite a little. The glands at the angles of the jaw are now enlarged to the size of almonds and are distinctly tender. There is also enlargement and tenderness of the cervical glands. The eruption has become fainter and more confluent on the legs and forearms and has extended to the hands, and also from the legs upward to the thighs and buttocks. In the latter region the exanthem is intense and of a morbilliform character. There is more eruption on the back and chest, in which region it has the form of discrete, lentil-seed sized, sharply defined macules. There is to-day some macular eruption upon the face. The uvula and soft palate are slightly injected.

18th. The temperature this A.M. is 100½° F. The patient is perspiring and complains of chilliness and pains in the back, arms, and legs. The eruption is now faint on the arms and legs, but is still quite con-

spicuous on the back and chest. The patient vomited last night and again this morning.

19th. The temperature last night was $101\frac{4}{5}^{\circ}$ F. and this AM. is $100\frac{2}{5}^{\circ}$ F. Patient is feeling better. The eruption is still well marked on the chest and back, where it shows many crescents. It is more pronounced on the face to-day than at any previous time.

20th. The eruption is still present on the back and chest, but is fading. There is still a little fever.

21st. Temperature last night was $99\frac{3}{5}^{\circ}$ F. This A.M. it is $99\frac{1}{5}^{\circ}$ F. The patient is feeling much better; the appetite is returning. The eruption has practically disappeared.

There were many anomalous features in this attack, among which may be mentioned the long and severe prodromal symptoms, the origin of the eruption on the legs, the complete absence of catarrhal symptoms, and the distinctly morbilliform character of the eruption.

COMPLICATIONS AND SEQUELÆ OF RUBELLA.

Rubella and chickenpox rank together as exhibiting the lightest incidence of complications of the various exanthematous diseases. There is no special complication liable to develop during the course of rubella, and in the vast majority of cases there are none.

Bronchitis and *pneumonia* have been mentioned by some writers. Edwards saw three attacks of pneumonia among 166 cases and Griffith observed two in 150 cases. Ryle and Edwards have each reported a case of *pleurisy*. Reference to *enteritis* and *enterocolitis* has already been made. Severe *secondary sore throat* has been reported by Tongue-Smith, Emminghaus, and Eustace Smith.

Hatfield reports 2 cases of *stomatitis* and Edwards 4 cases. Earle and Edwards make mention of *aphthæ*, the latter noting it in 30 cases.

Rheumatism was seen once by Slagle and Edwards, and several times by Earle. *Endocarditis* has likewise been observed.

Several cutaneous complications have been recorded. Alexander records 5 cases of facial *erysipelas*; *urticaria* is mentioned by Slagle, Earle, and Cullingworth; *febrile œdema* and œdema of the legs have been described. *Miliaria*, *furunculosis*, and *pemphigus* have been recorded as rare complications.

Blepharitis, *conjunctivitis*, *phlyctenular keratitis*, and *otorrhœa* have been met with. Mettenheimer speaks of *chronic nasopharyngeal catarrh*, *permanent swelling of the tonsils*, and *gingivitis*. Painful *enlargement of the thyroid gland* was observed by Slagle in 6 cases.

Albuminuria.—Hatfield found albumin in the urine twice and Cuomo three times. Kingsley, Cheadle, Duckworth, and Reed each record a case. We noted transient albuminuria in a case of rubella sent into the scarlet-fever wards as a case of scarlatina; the patient clearly had rubella and was discharged in ten days. In an attack of rubella in a girl suffering from postscarlatinal nephritis, swelling of the eyelids and legs followed the disappearance of the eruption.

In a series of 166 cases seen by Edwards albuminuria was present in about 30 per cent., but in the next 100 cases but 3 per cent. showed albumin. In the first series 9 cases presented well-marked albuminous urine, with dropsy. In none of the cases could tube casts be found.

Most of the complications above described excite interest rather because of their rarity.

Association with Other Diseases.—We have observed 100 cases of rubella occurring in children convalescent from scarlet fever. In none of these cases did it occur earlier than the fourteenth day of the disease and usually considerably later. (About one-half of these children had previously in their life had measles.) We have also seen rubella in children convalescing from a mixed attack of scarlatina and diphtheria.

In one little girl still scaling from scarlet fever, and showing the crusts of a profuse chickenpox eruption, a well-marked eruption of rubella appeared.

Relapse.—We have never observed a relapse in rubella, and from the absence of reference to such instances on the part of most writers it is evident that such occurrences are uncommon. Nevertheless, competent observers have recorded instances of recurring outbreaks. Emminghaus reports relapses in 3 cases and Earle in 2 cases. Edwards noted it once on the fourth day and once on the twentieth. Griffith noted a recurrence once at the end of eleven days and twice after a period of three weeks. Köstlin, Lindwurm, Golson, and Kingsley have also testified to the occurrence of relapses. The recurrent attack may equal the original in the intensity of its symptoms or it may be milder.

There does not appear to be a single authentic case recorded of actual *second attack*—i. e., due to a second infection and occurring after a period of months or years. It may, therefore, be said that one attack of rubella offers protection against subsequent infection.

THE DIAGNOSIS OF RUBELLA.

The diagnosis of an atypical case of rubella, particularly when occurring sporadically, may be attended with the greatest difficulty. In its classic form and especially during epidemic prevalence the diagnosis is a very simple problem. There is no one symptom which in itself is characteristic; the diagnosis must be made from a consideration of the composite symptomatology.

Measles. Measles is the disease which bears the closest resemblance to rubella, and which has, doubtless, been most often confounded with it. The differential diagnosis between these two diseases may be prefaced by the remark that a morbilliform exanthematous affection occurring as an epidemic among children who have had measles is in all likelihood rubella.

A confusion between measles and rubella may arise when the former disease presents itself in very mild form or when rubella appears, as it sometimes does, with severe manifestations. The history as to the

previous occurrence in the patient of measles or rubella is evidence of an important character. It is uncommon for measles to attack an individual twice and still rarer for rubella to act in this manner.

The incubation period of rubella is from five days to three weeks. Griffith regards the variable duration of this stage as compared with the fixed incubation period (about ten or eleven days) of measles as a feature of diagnostic importance.

The prodromal stage is very brief, rarely lasting more than twenty-four hours, or it may be absent altogether. Slight conjunctival redness, sneezing, and sore throat may be present. In measles there is a distinct pre-eruptive stage characterized by considerable fever and marked catarrhal symptoms affecting the eyes, nose, larynx, and bronchial tubes. The catarrhal symptoms are more pronounced in mild attacks of measles than in severe attacks of rubella. Some redness of the throat is usually present in rubella, whereas in measles sore throat may be absent.

Pinkish pinhead-sized elevations are at times observed upon the soft palate in rubella. The buccal mucous membrane sometimes exhibits reddish spots. The bluish-red spots surmounted by whitish dots described by Koplik as characteristic of measles are not seen in rubella.

Fever in rubella usually ranges from 99° to 101° F., rarely exceeding this. In measles fever is a prominent symptom, commonly registering 103° F. or more. It is much more protracted in measles than in rubella.

The eruption in rubella spreads more rapidly, fades on one part while spreading to another, and is of brief duration (one to three days). It consists of discrete, pale rose-red, slightly elevated, pinhead to pea-sized macules. In measles the eruption spreads more slowly, reaches a maximum intensity simultaneously all over the body, and lasts for four or five days or longer, being followed by a staining of the skin. The color is a deep red, at times being bluish. The macules are larger than in rubella, irregularly grouped, often being disposed in crescents, and presenting a distinctly blotchy appearance.

Glandular enlargement occurs in both diseases, but is more prominent in rubella, intumescence and tenderness of the postauricular and post-cervical glands being frequently present.

Measles is not infrequently complicated by pneumonia, an occurrence which is extremely rare in rubella.

Children with rubella are often so little disturbed as to complain about being put to bed. Measles is accompanied by an amount of prostration and weakness which cause the patients to seek their beds.

The above differentiation will suffice for ordinary cases. We occasionally encounter, however, attacks of measles which present anomalous features. The fever may be extremely slight, the eruption may be poorly marked, or the catarrhal symptoms may be almost in abeyance. On the other hand, severe cases of rubella are occasionally met with; conjunctival redness, coryza, and cough may be developed to an unusual degree, and the fever may be high. In other cases the eruption may be deep red, the macules may be arranged in crescentic groups, the rash persisting for five or six days. We have seen at least one case in which

the eruption could not be distinguished from that of measles, in this instance, however, catarrhal symptoms were absent. It is extremely rare to find a case of rubella which in all respects answers to the description of a normal case of measles, and it is still rarer to find a series of cases which fulfill this requirement.

Scarlet Fever.—It is quite possible to confound one form of the eruption of rubella with that of scarlatina. Many writers have acknowledged their inability to distinguish at times between the confluent scarlatiniform type of rubella and the scarlet-fever exanthem. In these cases other symptoms than the skin appearance must be relied upon for the differential diagnosis.

The incubation period of scarlet fever is distinctly shorter than that of rubella, lasting ordinarily from three to seven days. The invasive symptoms are sudden and quite severe; vomiting occurs in the majority of cases, followed by rapid rise of temperature, usually to 103° or 104° F. There is marked sore throat, the tonsils, soft palate, and uvula being particularly affected. The glands generally are enlarged, but more especially at the angles of the jaw. The tongue is at first coated, later exhibiting the characteristic red, papillated appearance.

The eruption appears first on the neck and upper chest; the face usually shows the circumoral pallor. The eruption lasts ordinarily five to six days. Desquamation occurring in flakes and most marked on the hands and feet is quite uniform. Middle-ear disease and albuminuria are extremely common complications.

It will be seen that the symptomatology is quite different from that observed in rubella. In the latter disease there is no vomiting, except in rare cases; the temperature is seldom high; the eruption begins on the face and is of short duration; the "strawberry tongue" is absent; sore throat is usually mild; desquamation when present is branny; complications are extremely rare. In addition the presence or absence of an epidemic of rubella or scarlet fever will greatly aid in arriving at a correct diagnosis.

Influenza.—Forchheimer states that in the epidemic of influenza in 1892 many cases were observed in which the differential diagnosis between scarlatina, rubella, and influenza presented difficulties, at least in the beginning.

There may be present in influenza an erythematous eruption, which may be localized or which may rapidly spread over the body. The fever, prostration, severe gastrointestinal or respiratory symptoms and the known prevalence of the disease will serve to distinguish it from rubella.

THE PROGNOSIS OF RUBELLA.

The prognosis is absolutely favorable in the vast majority of cases. Deaths have been so uncommon as to attract attention by their rarity; they have invariably been due to complications usually affecting the respiratory tract.

The mortality depends somewhat on the type of the epidemic and

the previous condition of health of the patients. Destitute and poorly nourished children are more apt to suffer from complications. Edwards had a mortality of $4\frac{1}{4}$ per cent. among a series of 150 cases occurring in a destitute class in a hospital. There were five deaths in 165 cases; 2 died of pneumonia and enteritis, 2 of enterocolitis, and 1 of tuberculous meningitis. Among his private cases he never saw a death.

Hatfield records a mortality of 9 per cent. occurring among patients in bad sanitary environment. Hemming, Alexander, Cuomo, Slagle, Roberts, McFarlan, Davis, and Forchheimer have each reported deaths, the last-named writer as a result of nephritis.

In about 100 cases observed by us in children convalescing from scarlet fever there were no deaths and no complications worthy of mention; indeed, the illness, almost without exception, was of a most trivial character scarcely necessitating the detention of the children in bed.

THE TREATMENT OF RUBELLA.

What has been said in connection with varicella is equally true of this disease; it is questionable whether it is necessary to isolate rubella patients in their homes. The disease is so mild, and in individuals in average health so devoid of complications and mortality, that such persons might be allowed to take it when it appears in their home. In hospitals it is proper to isolate patients with rubella, for here it may be inadvisable to superadd to another disease any infectious malady, however mild. The same may be said of institutions in which there are children in depraved health.

The only treatment that is necessary in the majority of cases is the guarding of the patient against undue exposure. Where fever is absent and catarrhal symptoms slight, one need not insist on rest in bed, although the child should be kept in a properly heated and ventilated room. The diet should be regulated according to individual requirements. No special medication is required unless the attack be severe or some complication develop.

If it be desirable to protect others from infection the patient should be isolated for about a fortnight.

CHAPTER XI.

TYPHUS FEVER.

Definition.—Typhus fever is a specific, acute, infectious disease, characterized by a continued fever of about two weeks' duration, pronounced nervous and brain symptoms, and by the appearance on the fourth or fifth day of a macular eruption which tends to become hemorrhagic.

Synonyms.—*Spotted fever, petechial fever, ship fever, jail fever, putrid fever, brain fever, camp fever.* Latin, *febris typhus; typhus exanthematicus*; French, *le typhus*; German, *Exanthematischer typhus, Flock fieber*; Italian, *il Tifo*.

History.—It is impossible to fix with accuracy the date of origin of typhus fever. The name "typhus" is mentioned in one of the Hippocratic essays, but it was applied at this period to acute fevers in general, accompanied by stupor and disturbance of the mental faculties. Many writers are of the opinion that Hippocrates actually observed cases of typhoid fever.

According to Hirsch, the first clear evidence of the occurrence of typhus is given by Fracastorius, a physician of Verona, who carefully chronicled the great pestilence which began in Cyprus and swept Italy on several occasions between the years 1805 and 1830. He distinguished this malady, which he called *morbus lenticularis*, from the plague. After devastating Italy, the epidemic spread to France, Spain, Germany, and other European countries. Some writers claim that typhus was unmistakably seen and described by Jacobus de Partibus in 1463 and by Agricola.

Typhus prevailed in extensive epidemics in different parts of Europe in the seventeenth century. During all this time it was confounded with typhoid fever. Indeed, these two diseases were not generally accepted as separate entities until almost the middle of the nineteenth century.

Much credit is due to that splendid clinician, Hildenbrand, of Vienna, for the pioneer work in clarifying the medical comprehension of these fevers. While Hildenbrand alludes in particular to the epidemic typhus of 1806, he states that he had been studying the disease for upward of twenty years.

Two fearful agencies of destruction, war and pestilence, have ever travelled in company. Conquest has often been purchased at a frightful sacrifice. Armies have carried home the laurels of victory, but also death-dealing plagues. Almost every great European war from the time of Charles the Fifth, in the middle of the sixteenth century, to the Turko-Russian conflict in 1878, has had its epidemic of typhus fever.

The Napoleonic campaigns saw thousands of France's soldiers perish by the hand of this ruthless enemy. According to Michaeli,¹ no less than 100,000 Russian soldiers in the Turko-Russian War contracted typhus; of this number, about one-half died. The mortality was particularly high among surgeons, 60 per cent. of the stricken succumbing to the disease.

In 1799, Rasori described a disease prevailing in epidemic form about Genoa. Although the designation "petechial fever" was given to this malady, it is evident that it was typhus.

The widespread military expeditions of the early years of the nineteenth century served to disseminate typhus throughout Europe. The disease later subsided, only to reappear from time to time in certain localities. Ireland has suffered many decimating outbreaks, and has been for many years the home of typhus fever.

Scotland and England have also frequently experienced the blighting influence of this scourge. According to Murchison, one million persons were attacked by typhus in England in the epidemic of 1847.

Germany has suffered frequent epidemics, the disease being usually imported from the Russian frontiers.

France has had a greater exemption from typhus than most of the other European countries. The disease nevertheless prevailed extensively during the Napoleonic wars, and at infrequent intervals since then.

The eastern seaport towns of the United States—New York, Philadelphia, Boston, Baltimore, etc.—have seen occasional epidemics of typhus fever, the disease being brought in by immigrants.

According to Licéaga,² an epidemic of fever marked by a spotted eruption ravaged Mexico in 1530. As this was coincident with the epidemics of typhus in Spain about this time, the view is reasonable that this disease was probably typhus. In 1545 another severe epidemic, in all probability typhus, swept Mexico, destroying eight hundred thousand lives.

Typhus fever is endemic in the large cities of the central plateau of Mexico; it increases in the winter months and not infrequently assumes epidemic proportions.

Among the most important contributions to our knowledge of the disease may be mentioned the writings of Sir John Pringle, Hecker, Rasori, Hildenbrand, Hufeland, Larry, Armstrong, Horn, Roupell, and, more recently, Murchison, Virchow, Lindwurm, Wood, and Griesinger.³

In the United States the writings of Gerhard and Pennock⁴ are deserving of special praise. Curschmann says: "To two American physicians, Gerhard and Pennock, belongs the credit of having finally established the differentiation (between typhus and typhoid fever). The

¹ Quoted by Curschmann, Nothnagel's Encyclopedia of Practical Medicine, Amer. ed., 1901.

² Article on Typhus Fever, Twentieth Century Practice of Medicine, 1898.

³ Curschmann gives full bibliographic references to the modern literature of typhus fever, and Murchison the literature before 1865.

⁴ On the Typhus Fever which Occurred in Philadelphia in 1836, Showing the Distinction between it and Dothienteritis, The American Journal of the Medical Sciences, 1837, vols. xix. and xx.

clearness of their differential diagnostic statements is noteworthy for their time."

Geographical Distribution.—Ireland and England (more particularly the former) have always been the home and distributing centre of typhus fever. This pestilence has been almost continuously present in these countries, exhibiting from time to time violent epidemic outbursts. The aggregate loss of life in Ireland from this disease has been appalling. Typhus fever has fortunately declined in recent years.

The Russian provinces bordering on the Baltic Sea and Poland have also been for years typhus-stricken territories.

In Germany the disease is usually limited to the southeastern provinces and to upper Silesia, although in times of epidemic prevalence Prussia also suffers. Germany receives its infection almost exclusively from the Russian borders.

In France typhus fever is seldom widely diffused, although it is said to persist endemically in certain parts of Brittany.

The disease is endemic to a certain extent in Northern Italy and also in Sicily and the neighboring islands. During periods of epidemic extension the entire country is overrun, as well as the lower provinces of Switzerland.

Austro-Hungary has its endemic centres in Galicia, Silesia, Moravia, and Bohemia. The disease is practically never extinct in Turkey, nor in Persia and China. India is comparatively free from typhus and the northern coast of Africa suffers only at times, with the exception of Algeria, in which country the disease has become endemic.

Spain and Portugal appear to be protected by their peninsular isolation and enjoy a relative degree of freedom from typhus.

Ireland and Russia represent the two important hotbeds of the disease. From these centres the disease is carried from time to time to the Central and Northern European countries, and to America. Irish emigration has frequently brought the disease to New York, Philadelphia, Baltimore, and other ports of the United States, but typhus has never gained a permanent footing in this country.

The disease persists endemically in the large cities of the central plateau of Mexico. In these densely populated districts typhus is never absent and epidemic outbreaks occur not infrequently.

THE ETIOLOGY OF TYPHUS FEVER.

Typhus fever is an infectious disease due to a specific cause, the nature of which has not been definitely determined. As a necessary corollary to this proposition it must be accepted that the disease spreads from one individual to another through the transmission of the typhus germs; this may take place directly or through the intermediation of infected articles.

The doctrine of the spontaneous origin of typhus fever, confidently asserted not many years since, dies with the acknowledgment of the germ genesis of the disease. It is now universally recognized that under-

feeding and overcrowding do not cause typhus, but merely favor its development and dissemination.

Contagiousness of Typhus.—Typhus fever is an extremely contagious disease, resembling in this respect the eruptive affections, such as measles, scarlet fever, and smallpox. Inasmuch as it is accompanied quite constantly by a cutaneous eruption of uniform character, there is good reason to include typhus among the exanthemata.

While typhus is an extremely transmissible disease, its infection is not so readily conveyed to others as is that of measles or smallpox. The chances of contracting the disease are directly proportionate to the frequency, duration, and intimacy of the exposure and to the degree of concentration of infection in the atmosphere.

Ventilation is a most important matter in lessening the dissemination of the disease. The poison of typhus fever commonly requires a certain degree of concentration to acquire an active infectiousness. The intensity of the infection may be greatly diminished by the free admixture of air. In a well-aired hospital ward containing but a few patients the danger of contracting the disease is by no means as great as when the reverse conditions prevail.

When a previously unattacked individual enters a hospital ward in which a large number of typhus patients are being treated, or in a small and poorly ventilated sick-room, the liability is great that he will contract the disease.

While the disease may be acquired after a very brief contact, experience teaches that the frequency and duration of the exposure exert a considerable influence upon the chances of infection. Nurses who are continuously and intimately in attendance upon the sick run the greatest risk. During the Crimean War, within a period of fifty-seven days, 603 nurses out of 840 in the service contracted typhus. In the Turko-Russian conflict all of the Sisters of Charity and 80 per cent. of the orderlies were attacked.¹

The incidence of typhus in hospitals is greatest among nurses, next among resident physicians and students, then among visiting physicians, and, finally, among officials who make but occasional visits.

Anderson² states that at the Fever Hospital at Glasgow, and in the English Fever Hospitals generally, the assistants rarely escape the disease.

Stokes and Cusak³ are authority for the statement that from 1813 to 1846 in Ireland there were among physicians 568 cases of typhus and 132 deaths, constituting approximately 46 per cent. of all cases and 10.5 per cent. of the deaths. Sixty per cent. of the surgeons in the Russo-Turkish War were stricken by the disease.

There is perhaps no disease which attacks physicians and nurses in such large numbers as typhus fever. Yet when but few patients are treated in well-ventilated wards the danger is slight. On several occa-

¹ Mentioned by Licéaga, loc. cit.

² Quoted by Licéaga.

³ Ibid.

sions a few typhus patients have been treated in the Municipal Hospital, and neither physicians nor nurses have contracted the disease. Lebert says that in 1868 and 1869 typhus was not propagated in his hospital wards, which were carefully ventilated even in winter.

The *mode of dissemination of the contagium* of typhus is not definitely known. Its poison resembles that of the exanthematous diseases in that it is apparently contained in the exhalations from the patient and attaches itself readily to articles brought into contact with the sick or in his immediate neighborhood.

That the contagium is frequently imparted to the underclothing is proven by the frequency with which washer-women, who have cleansed the bed and body linen of typhus patients, have contracted the disease. Indeed, the number has been so great in some epidemics that women could no longer be secured to undertake this work.

Curschmann says that it seems doubtful, or at any rate unproven, that the contagium is excreted in the bowel movements and urine. On the other hand, Licéaga states that "infection through fecal matter in process of decomposition is the only cause to which could be attributed many small epidemics," and, further, "individuals have contracted typhus fever at a time when it did not prevail epidemically, after having breathed in the effluvia from a water-closet, a drain, a sewer, or a recently opened excavation in an infected soil." The importance attached to this source in Mexico is evidenced by the reports of the sanitary inspectors of the City of Mexico, who allege that typhus fever could be attributed to emanations from fecal matters in process of decomposition in 1108 cases out of a total of 5749 inspections.¹

The infection is also believed by some to reside in the desquamated epithelium, in the sputum, and in other secretions and excretions. Until the typhus germ is discovered, the determination of the residence of the infection must remain a matter of conjecture.

The disease is *most contagious* during the febrile period and particularly at the acme thereof. The contagiousness appears to progressively lessen with the decline of the disease and becomes extinguished during convalescence.

Curschmann considers transmission of the disease possible during the period of incubation and absolutely certain during the initial stage.

After convalescence is established, the disease may be propagated through infected articles. The infection may be carried by well persons in clothing, a fact which should be borne in mind by physicians and nurses in attendance upon typhus patients. The infection may cling to objects for a long time. A remarkable example of the transmission of the disease through infected objects is given by Pringle.² During the invasion of Germany by English troops in 1743, a number of tents which had been used for typhus patients were sent to Gand for repair. The workman and 23 assistants working upon the tents fell ill with

¹ Mentioned by Licéaga.

² Quoted by Licéaga, loc. cit.

typhus fever and 17 of them died. Gand was at that time free of typhus fever and the workmen had had no communication with typhus patients.

Doubtless many of the alleged cases of spontaneous origin of the disease in prisons and on board ships have been due to the presence of an unsuspected contagium in clothing or baggage.

Typhus fever is *not spread* to any extent by *aërial transmission*. It is the common experience of those in charge of typhus fever hospitals that the disease is not carried to the surrounding domiciles. Furthermore, the disease is rarely conveyed from one household to another upon the opposite side of the street, even though the intervening distance be very small. The striking distance of typhus appears to be limited.

Epidemics of typhus are much more common in the cold than in the warm months. In Mexico and other countries in which the disease is endemic, epidemic recrudescences occur during the *winter* season. Curschmann regards the winter outbreaks as a result of the mode of living at this time of the year.

But few persons seem to possess a natural immunity against typhus. The vast majority of persons will, when exposed to a concentrated infection, contract the disease. Many, however, will escape when the infection given off is attenuated.

One attack of typhus protects against subsequent attacks in the majority of cases. There are, to be sure, exceptions which occur about as frequently as in the other exanthematous diseases.

Sex.—Sex appears to exert but little influence upon susceptibility to the disease.

Age.—Typhus attacks persons of all ages, except possibly infants at the breast, who exhibit about the same degree of insusceptibility to this disease as to the other exanthemata.

The disease is most common in youth and in early and middle adult life, from the ages of ten to forty years. The very aged are not spared, for persons over the age of eighty are every now and then attacked.

There are certain factors, such as underfeeding and overcrowding, which must be regarded as strong *predisposing and contributory causes of typhus fever*. Typhus is most prevalent in those localities where poverty and all that it entails is most pronounced. In Ireland epidemics have repeatedly followed failure of crops and its resulting famine and distress.

Dr. Osborne, describing the privations of the Irish people and their relation to typhus, in 1816 and 1817, says: "Families consisting of many individuals were found in garrets and cellars, with no covering but the remnants of clothing too contemptible for even the pawnbroker's avarice, water their only drink, and food, if any, the offal collected from the slaughter houses."

Brittany appears to be the only province in France in which typhus has shown a tendency to become endemic, and the poverty of this province is similar to that of Ireland. In Silesia much the same conditions prevail.

Overcrowding.—Overcrowding plays an important part in the spread of typhus fever, doubtless by effecting a concentration of the poison and favoring its transmission to many individuals. Therefore, the disease commonly breaks out in prisons, barracks, lodging-houses, ships, and badly constructed hospitals. The two English cities which are most densely populated, and in which people are most crowded in restricted quarters, are Liverpool and London, and these cities are those which habitually have most typhus.

Susceptibility to typhus fever is greatly increased by debilitating influences, which lower the resisting power of the individual. Physical exhaustion, mental anxiety, intemperance, underfeeding, exposure, and all the accompaniments of poverty and misery are included in this category. In addition various acute and chronic diseases may act as strong predisposing causes.

Typhus fever more than any other disease follows in the path of war and famine; it is essentially a disease of the poverty-stricken and miserable.

THE BACTERIOLOGY OF TYPHUS FEVER.

No one at the present day would hazard a belief in the spontaneous origin of typhus fever. The epidemicity and general behavior of the disease indicate that typhus fever is transmitted by a micro-organism in the same manner as the other acute exanthematic diseases.

As is true of nearly all of the exanthemata at the present time, the microbic cause of typhus has not yet been isolated and positively identified. The recorded researches into the bacteriology of the subject will be briefly referred to.

Moreau and Cochez¹ in 1888 isolated a bacillus from the blood and urine of typhus patients which bore a resemblance to the typhoid organism.

A little later, Hlava, of Prague, found a streptobacillus in the blood of persons dead of typhus fever. Of 45 corpses examined, this organism was recovered from the blood in two-thirds; it could not, however, be isolated from the viscera. Hlava succeeded also in recovering this streptobacillus from the blood in a certain proportion of living subjects. The claims of Hlava, although conservatively expressed, were later disputed by Cornil and Babes.²

Kasan discovered in the splenic blood of typhus patients rounded bodies with filiform, motile prolongations, to which he gave the name "spirochetæ exanthematicæ." This appellation was also employed by Lewaschew in describing bodies found in the blood of the spleen and in smaller numbers in the general circulation. The organisms were minute, highly refractile, coccus-like bodies, some of which were shown to possess free flagellæ, like the typhoid bacillus.³

¹ Contrib. à l'étude du typhus exanth. Gaz. hebdom., 1888, No. 28.

² Étude sur le typhus exanth., Arch. Bohém. de méd., 1889, tome III.; also Centralbl. f. Bakt., 1890.

³ Ueber die Mikro-organismen des Fleck typhus, Deut. med. Woch., 1892, No. 18, also No. 34.

Thoinot and Calmette¹ found in the blood from the spleen of 5 cases of typhus, during life, a micro-organism which was at times flagellated and at other times amoeboid.

Calmette regards the bodies found by Hlava, Lewaschew, Thoinot, Babes, Brühl and Dubief, and by himself as different forms of the same organism.

Dubief and Brühl² isolated from the blood of 9 typhus patients, during the Paris epidemic of 1892 and 1893, a diplococcus which they called the "diplococcus exanthematicus." This was also obtained from the air passages and in the sputum. The organism is surrounded by a capsule and stains well with methylene blue. Upon ordinary culture media orange-yellow colonies are developed. The authors allege to have produced a typhus-like disease by inoculation of lower animals. Haushalter and Étienne obtained negative results in a search for this organism.

Le Gendre recovered from the blood of a typhus patient during life and from the viscera at autopsy a bacillus resembling the typhoid organism.

Gomez, a Mexican veterinarian, working in the laboratory of the Superior Council of Health, has come to the conclusion that the organism of bovine typhus is identical with that of human typhus.³

From the above observations it is evident that further research is necessary either to harmonize the findings already made or to bring new light to bear upon the parasitic cause of typhus fever.

THE PATHOLOGY OF TYPHUS FEVER.

Contrary to the statements of some of the older writers, there is nothing pathognomonic or characteristic of typhus fever in the autopsy findings. Such changes are present as would indicate the existence of an intense infectious process. Post-mortem results in typhus fever often have a negative value in excluding the possibility of the existence of typhoid fever.

When death occurs during the eruptive period, there will often be seen the petechial spots, which, according to their age, will present purplish, greenish, yellowish, or brownish coloration.

Where considerable ecchymotic exudation into the skin has occurred, incision through the patch will show the presence of blood in the corium. Occasionally hemorrhages take place into the muscles, later giving rise to circumscribed areas of necrosis and softening.

The severe cerebral symptoms might lead one to expect pronounced changes in the *nervous structures*. Nothing, however, peculiar to the disease is observed in the brain or its membranes. The meninges are usually the seat of marked congestion and not infrequently of hemorrhages, which may be extensive, although they are usually circumscribed.

¹ Notes sur quelques exam. du sang. dans le typh. exanth., Annales de l'Institut Pasteur, 1892.

² Contrib. à l'étude anat. path. et bact. du typhus exanth., Arch. de méd. expériment., 1894.

³ Mentioned by Licéaga, loc. cit.

Diffuse meningitis is a condition seldom encountered. The surface of the brain is hyperemic and the cerebral substance upon section shows numerous dots of blood. The cortex of the brain is rather softer than normal and slightly oedematous. A subarachnoid effusion is nearly always present, being clear, turbid, or sanguinolent in character. The same is true of the ventricular fluid, which is not infrequently increased in amount.

The spinal cord shows congestion of the pia mater and effusion into the subarachnoid space.

The changes in the cardiovascular apparatus are the same as those observed in other infectious fevers. The heart muscle is soft, flabby, and of a pale or yellowish-red color, indicating myocardial degeneration. One-sided dilatation of the heart is usually present. Endocarditis and pericarditis are of great rarity.

At times structural changes in the bloodvessel walls are noted. Not rarely thrombi are found adherent to the walls of the bloodvessels of the thigh. Embolic or thrombotic obstruction of the arteries of the extremities is occasionally noted, giving rise to gangrene of the parts supplied by the damaged vessels.

The frequent employment of venesection by the older physicians gave repeated opportunity for the study of the coagulability of the blood in typhus fever. The blood is darker than usual and shows a less tendency to coagulate than under normal conditions. Jiminez described the blood as resembling "a watery fluid holding in suspension a very fine powder of a dark-red color."

The respiratory organs are commonly the seat of pathological changes. The mucous membrane of the nose, pharynx, and larynx is congested, swollen, and often ulcerated. Ulcerations with formation of pseudomembrane may be seen in the pharynx or larynx, and, in rare cases, farther down the respiratory tract. Curschmann found intense laryngeal disease in 4 per cent. of the cases at autopsy. There was "marked reddening and swelling of the mucous membrane, with oedema and erosions or fissures, the last particularly on the posterior wall, on the epiglottis, and on the ventricular bands."

Unilateral perichondritis and necrosis of the arytenoid cartilage were associated with these changes. The trachea, bronchi, and bronchioles show evidence of severe catarrhal inflammation; the lining membrane is reddened, soft, and covered with an adherent, tenacious mucus.

Hyposstatic congestion of the base of the lungs is extremely common; the pulmonary tissue in this condition is devoid of air, no longer crepitates or froths, and is practically in a state of splenization.

Local pneumonia is common in some epidemics and rare in others; Curschmann says 15 per cent. of his autopsies discovered the presence of local pneumonia, and Laverge reports 7 cases of extensive pneumonia out of 21 examined. Hemorrhagic infarcts and gangrene of the lungs are at times observed.

Pneumy's comparison of pneumonia when it develops it may even make a comparison.

The chief interest in the alterations in the *digestive tract* attaches to the appearance of the intestinal mucous membrane. Many of the descriptions by the older writers of the ulcerations found in the bowel related really to cases of typhoid fever which were erroneously diagnosed.

In typhoid fever Peyer's patches are hypertrophied and ulcerated, the excavations at times extending to such depth as to lead to perforation of the bowel and the development of peritonitis. In typhus fever Peyer's patches are not involved, and the solitary follicles are likewise usually exempted. The mucous membrane is congested and occasionally punctated hemorrhages into the mucous membrane are noted.

The *stomach* is occasionally congested and may exhibit small hemorrhages into the walls; in rare cases there is ecchymotic extravasation and extensive softening.

The *liver* is often enlarged and hyperæmic and shows evidence of cloudy swelling.

The *spleen* is enlarged in a considerable proportion of cases, but the swelling is neither as pronounced nor as uniform as is the case in typhoid fever.

The *kidneys* frequently show evidences of congestion and cloudy swelling. Curschmann states that in the Moabit Hospital in Berlin, in 1878 and 1879, there were found 5 cases of pronounced recent parenchymatous nephritis among 80 autopsies.

THE SYMPTOMATOLOGY OF TYPHUS FEVER.

Period of Incubation.—The period elapsing between the reception of the poison and the true onset of the disease is usually devoid of symptoms. In a minority of cases mild manifestations of indisposition may be noted, such as *malaise*, loss of appetite, and vague aches.

It is somewhat difficult to accurately estimate the duration of the incubation stage, for persons do not always take typhus upon the first exposure. It is only when the contact has been single and brief that the length of the latent stage may be satisfactorily determined. Of course, every possibility of exposure to another source of infection must be excluded.

The average length of the period of incubation may be said to be *twelve days*. In a not inconsiderable number of cases it will be found to be four or five days less than this. The extreme limits of the period may vary from one, two, or four days to about two weeks. Much longer periods, extending to several months, have been mentioned by the older writers, but these have doubtless been based upon errors of observation. The retention of infection in bed-clothing, garments, baggage, or like articles might give rise to attacks of the disease which would be separated by long intervals from previous cases.

General Outline of the Symptoms.—The invasion of typhus is usually sudden and not heralded by prodromal illness. An abrupt rigor or a succession of chilly sensations marks the onset of the febrile period. Chilliness may persist for several days, seldom amounting, however, to

visible shivering. Nausea and vomiting are not infrequently present, but seldom continue long. Constipation exists in the vast majority of cases. The fever mounts rapidly and to a considerable height; ordinarily, the initial pyrexia registers 102° or 104° F. With the rise in the temperature there develop the usual associated symptoms of high fever—headache, vertigo, insomnia, muscular pains, and prostration. The headache, which is severe and unremitting, is usually located in the frontal and temporal regions, with often pronounced pain and tenderness in the eyeballs. Backache, chiefly in the sacral region, is sometimes a distressing symptom. Pains in the legs are not uncommon.

A frequent early symptom is *nose-bleed*, which is observed most commonly about the third day. It may vary in severity from a barely perceptible bleeding to an uncontrollable and even fatal hemorrhage, as in a case observed by Jiminez.

Tinnitus aurium is often pronounced, followed later by partial or complete deafness. The mind is usually clear in the beginning, although the patient exhibits but little interest in his surroundings.

The *facies* is so characteristic as to be of diagnostic value. The face is flushed, dusky, and sometimes slightly oedematous; the eyes are congested and heavy, and the expression dull and apathetic. There is evidence of great muscular relaxation, the patient lying prostrate upon his back. Sleep is interrupted by disturbing dreams, which cause the sufferer to start.

The temperature now continues its ascent, reaching its acme about the fourth or fifth day. With the increased pyrexia there is a corresponding augmentation of the pulse rate, which commonly reaches 100 to 120; in children the pulse is more rapid, acquiring a frequency of 140 or 150 to the minute.

About the fourth or fifth day the most characteristic symptom of the disease—the rash—makes its appearance. The true exanthem is, in some cases, accompanied or preceded by a morbilliform rash of transitory duration, analogous to the prodromal rashes of variola, vaccinia, etc. The typhus eruption is commonly seen first on the anterior surface of the trunk, and later on the back, arms, and legs. The face and palmar and plantar surfaces are usually exempted. The eruption consists of pinhead to lentil-seed sized, reddish spots or macules. These acquire from day to day a deeper coloration, finally becoming purplish and no longer disappearing under the pressure of the finger, thus evidencing a hemorrhagic extravasation into the skin. The number of lesions is at first small, but later the eruption may become quite profuse.

The full development of the exanthem marks the height of the morbid process. The symptoms have now acquired increased severity. The fever is at its maximum and the pulse is rapid; the tongue is parched, dry, and brown; the mouth half-open, the teeth covered with sordes, and the lips with blood crusts. A dry cough denotes the presence of a bronchitis, and rales may be heard upon auscultation. Catarrhal inflammation of the larynx may lead to hoarseness or aphonia.

The patient is profoundly prostrated, the lips scarcely moving on

speaking Apathy has been replaced by a delirium which in some cases is of a muttering character, but in others is violent or maniacal. Homicidal or suicidal efforts may be attempted and require the greatest vigilance upon the part of the attendants.

The patient is unable to hear, speaks in a scarcely audible tone, and is often too weak to protrude his tongue. Delirium, stupor, and semi-consciousness follow each other in irregular order. The abdomen is tense and somewhat tympanitic; constipation is the rule, but diarrhoea may set in toward the end of the disease, and the stools may be passed involuntarily. The bladder becomes paralyzed and incontinence or retention results. If the disease progresses to an unfavorable termination the temperature increases to 105° or 106° F., the pulse becomes rapid and feeble, the face acquires a livid hue, there is picking at the bed-clothes and tremor of the hands, increasing coma, and finally death from exhaustion.

Death may also result from the effects of wild delirium and physical exhaustion; in other cases a bronchopneumonia or hypostatic congestion of the lungs hastens the fatal outcome.

Recovery may occur in typhus fever even after the development of alarming symptoms. The disease is self-limited and not of protracted duration, and if the patient can be tided over the crucial stage rapid convalescence sets in.

When a favorable termination is to occur, a rapid defervescence in the temperature is noted about the fourteenth day; with the fall in the fever, the patient lapses into a refreshing slumber. The pulse diminishes in frequency and acquires more volume, the tongue becomes moist and loses its coating, the mental faculties clear up, the voice returns, and the patient expresses a desire for some food. The eruption gradually fades in color, the petechial lesions being last to disappear. Branny desquamation usually occurs at the site of the purplish maculæ and stains persist for a considerable length of time.

Deafness and prostration may continue for a while, but recovery from moderate cases of typhus is more rapid than would be expected from the formidable character of the symptoms.

Consideration of the Symptoms in Detail. **Fever.**—The intensity of the fever in typhus is an excellent index of the severity of the disease. The febrile curve has certain distinct characteristics which distinguish it from typhoid fever.

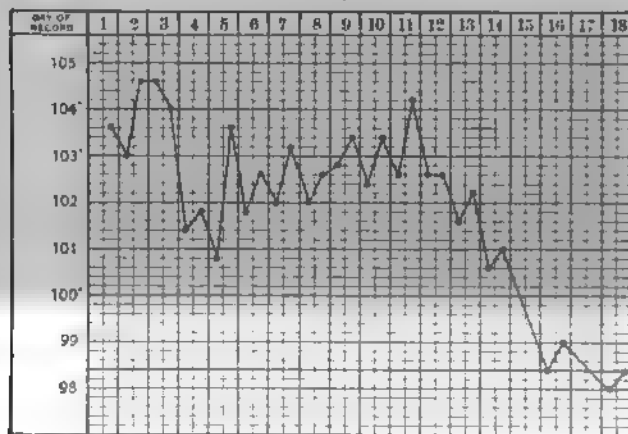
The pyrexia rises quite rapidly to a considerable degree, so that on the evening of the first day the temperature registers 102° or 103° F., and occasionally 104° F. Some of Wunderlich's cases exhibited temperatures from 104° to 104.9° F. With slight morning remissions, the fever continues its ascent on the second and third days, commonly reaching its maximum on the evening of the fourth. At this time the evening temperature in cases of moderate severity will be in the neighborhood of 104° F., whereas, in very severe attacks it may reach 105° or 107° F. The fever now remains at about the same level for four or five days, although a slight lowering of the temperature may be noticed in the

evenings. From the seventh to the ninth days an average evening temperature of 103° to 105° F. might be expected.

In favorable cases the fever begins to decline on the ninth, tenth, or eleventh day or a little earlier or later. In severe cases it may be postponed until the fourteenth, fifteenth, or sixteenth day. In desperate cases the fever may rise to great height about this period.

A day or so before the subsidence of the fever it is not rare to observe striking irregularities in the temperature curve. This precritical disturbance is sometimes characterized by a pronounced rise in the temperature to 105° or 106° F., and in other cases by a fall to normal or thereabouts. There is, however, a rapid rebound and the fever shortly afterward permanently abates. The fall in the temperature commonly begins in the evening and continues during the night. Critical declines may occur in some cases, the temperature dropping to normal in the course of

FIG 90



Case of typhus; gradual decline of temperature. Recovery (Doty).

twelve hours; more commonly, however, there is a step-like descent, requiring two, three, or four days to reach the normal line. It is seen, therefore, that the fever more often declines by lysis than by crisis. (Fig. 91.)

In fatal cases it is not rare to note a preagonic hyperpyrexia. Wunderlich observed a temperature of 109.4° F. just before death.

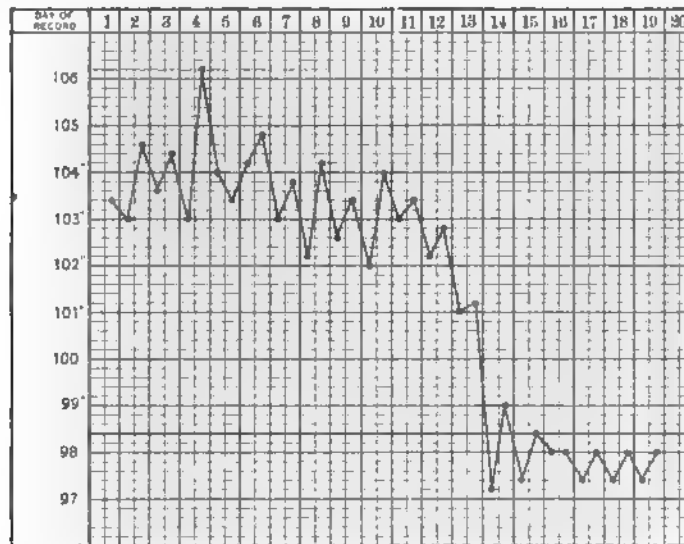
Pulse.—The frequency of the pulse in typhus fever, under ordinary circumstances, is proportionate to the intensity of the accompanying pyrexia. In this respect and in the rarity of dirotism it differs from the pulse of typhoid fever. In moderately severe cases the pulse rate in the evenings, during the first week, varies from 110 to 120. At this time the pulse is full and of good volume, but later becomes softer and more compressible. Dirotism is occasionally observed during the second week, but is distinctly rarer than in typhoid fever. In severe cases, as the disease progresses, the pulse becomes rapid, feeble and small,

and frequently intermittent. Patients may lie for a number of days with the pulsations scarcely palpable at the wrist.

The cardiac sounds are clear and of good tone early in the disease, but later, especially in severe attacks, give evidence of myocardial change. They may become weak and distant and the first sound almost inaudible. When this develops with accompanying cyanosis of the face and extremities acute dilatation of the heart is to be expected.

The Typhus Rash or Exanthem.—The eruption of typhus fever is so uniformly present and so characteristic of the disease as to warrant the inclusion of typhus in the list of exanthematous affections. It may in rare cases be absent, and in others so poorly defined as to escape observation. It has been estimated, however, that it is seen in 95 per

FIG. 91



Case of typhus; decline of temperature by crisis. Recovery (Doty).

cent. of all cases. It is one of the most conspicuous and diagnostic symptoms of the disease, a fact which has led to the use of such designations as "spotted fever," "petechial fever," etc.

The exanthem usually makes its appearance upon the fourth or fifth day of the disease, but may occur as early as the second and as late as the eleventh day. Salamon, working with Curschmann, observed the rash in 39 cases of typhus; of this number, it appeared 11 times on the fourth day, 13 times on the fifth day, and 5 times on the seventh day.

The spots appear first upon the abdomen, chest, shoulders, and back; very soon they make their appearance upon the arms and legs, even as far as the hands and feet. The face is usually entirely free of eruption, although in children at times the rash may be sufficiently pronounced to cause confusion with measles.

The lesions are not very abundant upon the first day, but constantly

increase in number for about forty-eight hours, when the full complement of spots is present.

The rash is made up of two elements—a background consisting of a poorly defined, violaceous reticulation, the so-called “subcuticular mottling,” and the rose spots or maculæ. The macules are pinhead to lentil-seed sized, pale red or rosy-red at the onset, with ill-defined borders and scarcely elevated above the surface of the skin. In some cases the mottling may be present without the spots, but the converse of this is seldom the case. In the beginning the macules disappear completely upon pressure, but gradually the color becomes more dusky or actually purplish and the discoloration can no longer be made to fade under tension or pressure. The bluish or purplish coloration is evidence of hemorrhagic extravasation into the skin. At times, late in the course of the disease, petechiæ may develop upon healthy areas of the skin without the previous presence of macules.

Only a certain proportion of rose spots become the seats of hæmic extravasation. In general it may be stated that the greater the extent of hemorrhage into the skin, the more severe is the attack. Petechial spots are most commonly seen about the flexures of joints, particularly the groin, and on dependent portions of the cutaneous surface, such as the back.

The duration of the eruption varies according to the amount of dermic hemorrhage. Simple rose spots may disappear in a day or two; those showing moderate extravasation fade in five or six days, while deep purplish petechiæ may persist for two or three weeks.

During the process of fading the spots pass through the color gradations of blood pigment, showing themselves as greenish, yellowish, or brownish stains. The disappearance of the eruption is commonly followed by a branny or furfuraceous scaling.

The individual lesions of the typhus eruption in the beginning bear a strong resemblance to those of typhoid fever. They are, however, less papular, more abundant, and later petechial in character. The macules are, at times, more abundant upon the extremities than upon the trunk, a circumstance that is never observed in typhoid fever; indeed, in the latter disease spots upon the arms and legs are quite unusual.

In exceptional cases the rash of typhus may be absent, constituting the so-called *typhus sine exanthemate*. Murchison failed to discover a rash only 55 times in 2499 cases.

Spleen.—The spleen appears, according to Curschmann, to be moderately enlarged in the majority of cases of typhus. The enlargement begins usually from the third to the fifth day and is determinable by palpation. The splenic swelling does not last long, but subsides usually with the decline of the fever. This explains the negative results that have been noted in autopsies, the swelling having disappeared before death.

Subcutaneous Lymphatic Glands.—The subcutaneous lymphatic glands are ordinarily not enlarged. In some epidemics the inguinal and

PLATE LVI.



Petechial Eruption of Typhus Fever upon the Trunk. Recovery

Patient was an immigrant treated in the Municipal Hospital

axillary glands have been observed to undergo inflammation and supuration. The parotid and submaxillary glands may become tumefied either early or late in the course of the disease.

Nervous System.—Psychic disturbances in typhus fever are among the most conspicuous and constant manifestations of the disease. Indeed, the word typhus is derived from a Greek term signifying stupor. Early in the disease the nervous phenomena play a prominent role in the symptom-complex.

Headache, intense restlessness, and insomnia are seen in nearly all cases. The cephalalgia is intense and persistent, seldom abating before the appearance of the exanthem, and frequently not until the end of the first week. Inability to sleep is a distressing symptom and one difficult to relieve; it often continues up to the critical period, when the patient falls into a refreshing slumber. Giddiness and noises in the ears commonly accompany the early headache; the former is rendered manifest when the patient assumes the erect position or even when he sits up in bed.

Consciousness is preserved during the early days of the disease, but there is a dulling of the mental faculties. The patient, though listless and apathetic, is able to pertinently answer questions addressed to him.

Gradually, however, the intellect becomes clouded, perception is slow, memory fails, and confusion reigns supreme. The patient loses knowledge of his surroundings and lapses into a semistuporous condition from which he can be but partially aroused.

As would be naturally expected, the headache, rachialgia, and other subjective disturbances gradually disappear as the psychic faculties are obtunded.

Delirium is a prominent symptom of the disease and usually manifests itself during the latter half of the first week. It varies greatly in its character, depending much upon the temperament of the patient and the nature of the psychic impulses which he experiences. At times it is of a muttering character, the patient talking incessantly in a low tone between his half-closed teeth. The sufferer frequently imagines himself in the performance of his usual duties and his conversation and actions will be governed accordingly.

Delusions of persecution are commonly experienced; the patient is suspicious of nurse, physician, and attendants; he refuses food for fear it is poisoned. He is apprehensive of all sorts of imaginary dangers, and may as a result attempt to make his escape, preferring, as a rule, the window as an avenue of egress. In other cases the patient may experience terrorizing hallucinations, and become aroused to the highest degree of maniacal excitement. Under the influence of these insane impulses self-destruction may be attempted or aggressive assault may be made upon the attendants.

Cases are on record in which patients have leaped headlong from windows in their suicidal endeavors. The greatest vigilance is necessary on the part of the attendants in the care of patients suffering from this disease.

In severe cases the delirium terminates in coma, which, in fatal cases, becomes progressively more profound. The tongue and hands are tremulous and there is twitching of the muscles and picking at the bed-clothes. When coma-vigil develops the patient is in a most desperate state; the patient neither sees nor hears, although the eyes are wide open and staring fixedly into space.

In rare cases epileptiform convulsions are observed, the patient lapsing into coma after the subsidence of the convulsive movements. This only occurs in the worst cases and is usually associated with the presence of considerable albumin in the urine.

In cases terminating fatally there is a progressively deepening coma from which the patient cannot be aroused. The patient is, of course, unable to swallow; urine and feces are passed involuntarily; the pulse becomes rapid, feeble, and intermittent; the respirations hurried and shallow, and death takes place from exhaustion.

Most writers refer to a *disturbance of hearing*, beginning usually toward the end of the first week and amounting in some cases to complete deafness. Curschmann claims that auditory disturbances do not make their appearance until the period of convalescence, when they become comparatively frequent.

He ascribes the deafness not to the action of the toxin on the auditory centres, but to a catarrhal otitis media which at times ends in abscess of the middle ear, with perforation.

Gastrointestinal Tract.—The tongue in the beginning is covered with a thick, whitish fur; later it becomes dry and brown. During the comatose state it is commonly hard and leathery and covered with dried blood which issues from the fissures. The mucous membrane of the mouth and lips is likewise dry and covered with sordes.

Thirst and anorexia are common symptoms at the onset of the disease. Vomiting is not common, but occasionally occurs during the period of invasion. In rare cases it may be repeated and accompanied by epigastric pain.

Constipation is the rule in nine-tenths of the cases during the first week. Later in the disease diarrhoea may set in and stools may be passed involuntarily. It is associated with meteorism and some abdominal tenderness. Loose movements are believed by many physicians to be due to the liquid diet upon which the patients are kept. The stools do not possess the distinctive character of the typhoid-fever dejecta.

Respiratory Tract.—A catarrhal condition of the entire respiratory tract, but especially the bronchial tubes, is so commonly seen in typhus fever as to belong properly to the symptomatology of the disease.

This process involves the nasopharynx, larynx, trachea, and bronchial tubes to their smallest ramifications.

Bronchitis.—Bronchitis is usually present during the first week; the cough is, as a rule, slight and accompanied by little or no expectoration. In the second week the bronchitis may become more widespread, and, through involvement of the terminal bronchioles, lead to atelectasis or bronchopneumonia.

Hypostatic Congestion.—Hypostatic congestion of the lungs is not uncommon owing to the recumbent position in which the patient persistently lies.

Bronchopneumonia.—Bronchopneumonia and lobar pneumonia are common complications and are not infrequently overlooked owing to the gravity of the more conspicuous symptoms. In addition, pain, cough, and expectoration may be slight or absent. Lividity of the face and an increase in respiratory frequency are suspicious symptoms. The lungs should be carefully auscultated from time to time to discover pneumonia or hypostatic congestion in their incipency.

Lobular or lobar pneumonia is a frequent cause of death, particularly in some epidemics.

Laryngitis.—Laryngitis is present quite commonly and gives rise to hoarseness and at times aphonia. Ordinarily this is due merely to a catarrhal inflammation of the laryngeal mucous membrane. In severe cases erosions and ulcerations may occur and lead to perichondritis and necrosis of the thyroid cartilage.

Kidneys and Urine.—The urine in typhus fever does not present any characteristics peculiar to the disease. As is the case in other febrile infectious diseases, the urine is of high color and specific gravity and shows an increase in the amount of urea and other solid organic constituents.

In cases with high fever a moderate febrile albuminuria is observed during the height of the pyrexia. This may be accompanied by the presence of a few hyaline casts.

True parenchymatous nephritis, evidenced by pronounced albuminuria, epithelial and hyaline casts, and at times blood, is fortunately an uncommon complication.

In 15 cases of typhus, the urine examined throughout the course of the disease is said by Buchanan¹ to have shown the presence of albumin in but 2 cases. Morales, cited by Licéaga, made 200 analyses of the urine and found albumin frequently. He furthermore noted the presence of peptone, urobilin, and the biliary acids. On the fifth day of the disease hyaline casts and pigment granules were commonly found.

COMPLICATIONS AND SEQUELÆ.

In addition to bronchopneumonia, nephritis, otitis media, etc., which were referred to under the head of symptomatology, there are other complications which occur from time to time during the course of typhus fever.

Bed-sores.—Bed-sores are not infrequently observed in dependent areas subjected to pressure. Curschmann found this complication present in about 3 per cent. of his cases. The supine position constantly maintained by typhus patients favors the development of a necrosis of the skin over the back, particularly in the region of the sacrum.

¹ Article on Typhus, Reynolds' System of Medicine.

Gangrene.—Gangrene of the skin, particularly of terminal members, such as the toes, ears, and fingers has been noted by a large number of physicians. When gangrene of the lower extremities develops, there are pain and numbness in the limbs, followed by a lowering of the temperature of the affected parts. The pulsations in the arteries cease and the toes begin to exhibit a livid hue, which later becomes purplish and finally black. The skin and subjacent tissues become hard and dry and mummification sets in. A line of demarcation may form and spontaneous amputation result, or surgical removal may become necessary. In some cases the sphacelation may take the form of a moist gangrene.

Noma.—Noma, or cancrum oris, occasionally develops in the course of typhus fever, as it does in some other exanthemata.

The terminal gangrene above referred to is doubtless due to an arteritis with the formation of arterial thrombi. When the veins of the legs are attacked, with the production of a phlebitis, the affected members become hot and swollen and take on the ordinary appearance of a *phlegmasia alba dolens*.

Erysipelas.—Erysipelas is a complication much spoken of by the older writers, but it is much less common at the present day owing to the better hygienic conditions which prevail in modern hospitals.

Boils.—Boils and subcutaneous abscesses are met with more frequently in some epidemics of typhus than in others. They develop, as a rule, during the convalescent stage, which may be as a result thereof prolonged.

Parotitis.—Parotitis appears to be one of the most frequent complications of typhus. It is encountered with unusual frequency in certain epidemics. Schilling, of New York, in 1852, observed it in about 20 per cent. of his cases. This, to be sure, is an unusually high incidence. The inflammation may come on at any stage of the disease, but most commonly during the third week. One or both sides may be affected. In the majority of cases the inflamed gland goes on to suppuration. In some cases the submaxillary salivary glands enlarge and undergo abscess formation. These abscesses add considerably to the gravity of the disease.

Jaundice.—Mild attacks of jaundice are not rare in the course of typhus fever; in some epidemics the icterus has been so intense as to suggest the existence of some other disease with hepatic disturbance.

Other Complications.—Local or general paralysis, gangrene of the lungs, and suppuration of the joints might also be mentioned as among the rare complications of typhus fever.

Temporary Insanity.—Temporary insanity in one of its various forms has been known to persist for some time after convalescence from typhus. Roupell mentions the case of a woman, aged twenty-two years, who suffered from mania and who was confined in a lunatic asylum for several months after convalescence from the disease, ultimately making a complete recovery from the mental aberration.

Duration of the Disease and Variations in the Course.—The majority of writers are in accord that the duration of typhus fever under

ordinary circumstances is about fourteen days. It is not rare for the disease to run a course of one or two days longer than this period, or, on the other hand, to terminate a day or two before the fortnight is completed.

It is uncommon for the fever to persist in uncomplicated cases after the eighteenth day and distinctly rare after the end of three weeks. Lebert says that he has exceptionally seen "the duration of the disease prolonged to five or six weeks, not merely by complications, but also by protracted convalescence of a slight febrile character."

Curschmann has observed cases beginning with marked *hyperpyrexia* run an unusually protracted course to a fatal termination. Under such circumstances, the fever, very high in the beginning, may fall to normal or below, where it may continue for some days or a week before death takes place. A fatal termination may be delayed to the end of the second or the middle of the third week.

Various authors have described cases of typhus of unusual *malignancy* which terminated fatally in a few days; this form of the disease was designated *typhus siderans* by the older writers. The symptoms, in brief, are a severe chill, rapid rise of temperature to great height, repeated vomiting, severe cephalalgia and general pains, frequent small pulse, and rapid clouding of the mental faculties. The spleen is found to be distinctly enlarged in these cases. The eruption is wholly or in part suppressed. Death may supervene in the course of two or three days, and in rare cases, it is said, even within a day or two after the onset of the disease.

Hemorrhagic Typhus Fever.—Hemorrhagic typhus fever is an excessively rare variety. The invasive symptoms are of great severity and are followed about the third day by hemorrhagic extravasation into the skin in the form of petechiæ and larger ecchymoses. In addition hemorrhages occur into the conjunctivæ and from the various mucous surfaces—from the mouth, nose, kidneys, uterus, intestines, etc.

There is pronounced cardiac weakness, profound prostration, and, in some cases, gangrenous complications. These cases exhibit a striking parallelism with that form of hemorrhagic smallpox known as *purpura variolosa*.

Under the heading of *abortive cases* of typhus fever, Curschmann describes attacks characterized by a violent chill followed by a rise in temperature, which reaches its maximum in twenty-four to thirty-six hours. For several days the pyrexia persists as a continued or continued-remittent fever, then declining rapidly by crisis to the normal line, where it remains. In these cases the fever may have run its course by the fifth or sixth day or earlier. The accompanying symptoms may be severe and alarming, even after the temperature begins to fall.

The rash in these cases is usually scanty and of short duration. In those cases in which it is absent the diagnosis may be rendered extremely difficult and at times impossible.

Writers have referred to different varieties of typhus fever under such names as *inflammatory* typhus, *ataxic* typhus, *adynamic* typhus,

etc. These designations and many others have been used to classify certain expressions of the disease, but as they tend rather to complicate than to clear one's comprehension of typhus they might well be permitted to become obsolete.

THE DIAGNOSIS OF TYPHUS FEVER.

Although there is no pathognomonic symptom which distinguishes typhus fever from other diseases, yet the symptom-complex is sufficiently distinctive and well defined to render the diagnosis clear in the vast majority of cases.

The mode of onset, the rapid rise of fever to its maximum, the early development of pronounced cerebral symptoms, the peculiar facies, the characteristic rash, and the nature of the pyrexial curve collectively bespeak a disease which can be trenchantly separated from all other infectious maladies.

Typhoid Fever.—It is only within the last half-century that typhus has been clearly distinguished from typhoid or enteric fever. Exceptionally, individual cases still arise in which the differential diagnosis is difficult, but under ordinary circumstances these two diseases should not be confounded.

Typhus and typhoid fever prevail under different conditions, and spread in a different manner. The former is endemic in certain countries, but may reach other localities during epidemic prevalence of the disease. It is distinctly contagious and becomes disseminated through the contact of the well with the sick or through the intermediation of infected articles. Typhoid fever spreads in several ways, but chiefly through a contaminated water supply; it is not contagious, at least according to the usual acceptation of this term.

An attack of typhoid fever is usually preceded by a period of indisposition and *malaise*. Typhus fever, in the majority of cases, is ushered in suddenly and without prodromal illness.

The pyrexial curve varies considerably in the two diseases. In typhoid fever there is a step-like ascent for about a week, then about a week of even temperature, and finally a gradual decline occupying about the same period. The fever in typhus rises more rapidly, reaches its maximum about the fourth or fifth day, and declines to normal by a more or less critical fall about the end of the second week. The morning remissions are less pronounced than in typhoid, and the febrile course is, with rare exceptions, distinctly less protracted.

The pulse of typhoid fever is in general slower and more often exhibits dicrotism than the pulse of typhus. •

The chill, headache, pains in the legs, and prostration are all more intense in typhus. The nervous symptoms come on at an earlier date and the psychic disturbance, particularly the delirium, is more violent. The flushed and oedematous face, injected conjunctivæ, and general wild expression of typhus patients contrasts strongly with the pale, depressed countenance of typhoid patients.

The eruption of typhus develops earlier (about the fifth day), comes out in one continuous crop, and is usually more profuse than that of typhoid fever. It must be remembered, however, that the typhoid exanthem may occasionally be abundant and the typhus eruption sparse.

The rash of typhoid is generally limited to the trunk, whereas the typhus spots involve the trunk and extremities, even to the hands and feet. The typhoid spots come out in separate crops and are more papular and have a more defined border than typhus lesions. The latter, moreover, tend to become petechial, when they no longer disappear under pressure as do the typhoid rose spots.

Typhoid fever is more often accompanied by meteorism, gurgling in the right iliac fossa, diarrhoea, and the peculiar pea-soup stools.

The mean duration of typhoid fever is three weeks and of typhus two weeks. In addition to the above clinical symptoms, certain tests are of importance. The agglutination reaction of Widal will aid in the diagnosis of typhoid fever, but not during the early days. Eberth's bacilli may be recovered from the spleen, or from the urine, stools, blood, or rose spots. On autopsy Peyer's patches will be found to be ulcerated in typhoid fever, but not in typhus.

Relapsing Fever.—The differentiation of typhus and relapsing fever may be attended with great difficulty, particularly during the onset of the disease. In both maladies the fever rises rapidly to great height. Typhus, however, is accompanied by much more severe constitutional commotion and by greater mental disturbance; in relapsing fever the mind remains clear and the general condition remarkably good. Furthermore, there is entire absence of a cutaneous eruption. At the end of five or seven days in relapsing fever the temperature subsides to normal, where it remains for a similar period, then rising and ushering in the relapse. Jaundice is observed in a large number of cases. Examination of the blood will reveal the presence of the spirillum of Obermeier.

Malarial Fever.—In tropical countries and even elsewhere at times, a malignant form of remittent fever is seen which may in some respects closely resemble typhus fever. The high fever is accompanied by great prostration and early disorder of the mental faculties. Later, manifestations of the typhoid state may make their appearance. Where doubt exists the examination of the blood will reveal the presence of the hæmatozoa of malaria and the diagnosis will thus be rendered clear.

Meningitis.—Both in idiopathic meningitis and in the epidemic variety a similarity to typhus fever may be presented through the predominance of the cerebral symptoms. Cerebrospinal meningitis is, moreover, accompanied by an eruption which may lead to error. It is only, however, when the symptomatology is irregular that real difficulties in the diagnosis are presented. In meningitis the headache is more intense and of a sharp, boring character. Nausea and vomiting, which are rare symptoms in typhus, are apt to be present. Rigidity of the muscles of the neck and retraction of the head are of great diagnostic importance in meningitis. Later various paralyses develop.

Pneumonia.—In certain forms of pneumonia attended with typhoid manifestations and masked pulmonary symptoms, there may be a resemblance to typhus fever. The rash will be absent and a careful examination of the chest will discover the presence of consolidation of the lung.

Delirium Tremens.—Typhus fever occurring in persons strongly habituated to the use of intoxicating liquors may present symptoms simulating *mania a potu*. Insomnia, delirium, and muscular tremblings may be present in both conditions. The high fever, eruption, and course of the disease will readily distinguish typhus fever.

In the eruptive stage typhus fever may be confounded with measles, with hemorrhagic smallpox, and with severe forms of purpura.

Measles.—During the evolution of the eruption, the typhus exanthem, particularly when it is profuse, with a tendency to coalescence, may closely simulate that of measles. This is especially true in the case of children, in whom it may occasionally appear upon the face. Roupell believes that Sydenham was probably dealing with an epidemic of typhus fever in 1674 when he described an anomalous and malignant form of measles. Sydenham¹ says: "The measles of 1674 deviated from rule, did not preserve their type; the eruption came out irregularly, was often confined to the neck and shoulders. The bran-like desquamation did not result, peripneumonia more frequently took place, and in some cases the fever would last fourteen days or more.

Typhus differs from measles in many particulars, and may usually be readily differentiated. The prodromal stage of measles is characterized by marked catarrhal symptoms giving rise to sneezing and coughing; the fever rises gradually and not to such a height as in typhus; the face is profusely covered with the rash, which spreads downward over the trunk and extremities. In typhus the fever soon reaches its maximum, and the febrile course is longer. The rash seldom occurs on the face, the rose spots later exhibit petechial change, and the sensorium is more profoundly affected; patients previously attacked by measles are susceptible to the disease.

Smallpox.—The symptoms of the initial stage of smallpox and typhus fever present a striking similarity. In each disease we have chills, sudden high fever, headache, general pains, and profound prostration. Vomiting is much more frequent in variola than in typhus. The appearance of the characteristic eruption on the third day after the onset of the fever in variola will clear up the diagnosis. Between purpura variolosa and hemorrhagic typhus fever a differentiation is often impossible. Both are characterized by hemorrhages into the skin and from the various mucous membranes, associated with intense prostration and death in a few days. The knowledge of the prevalence of one or the other disease will aid in the diagnosis.

Purpura.—Severe cases of purpura hemorrhagica may likewise be confounded with malignant typhus fever. The former, however, is

¹ Opera, p. 232.

seldom ushered in with intense fever and the prostration in the beginning is not extreme. It is only under exceptional circumstances that a confusion of the two diseases would take place.

THE PROGNOSIS OF TYPHUS FEVER.

The wide divergence in the mortality rates of epidemics of typhus fever many years ago is doubtless due to the fact that typhoid fever, relapsing fever, and typhus fever were often confounded and considered one and the same disease.

The fatality of typhus is influenced by many factors, chief among which are the age of the patient, his hygienic environment, the condition of his health prior to the attack, and the severity of the prevailing type of the disease. These and other influences will be considered in detail.

Age.—The age of the patient influences the mortality to a considerable extent. With the exception of very young children the disease is much less fatal in childhood and youth than in age periods beyond these. Beyond the age of twenty years the mortality progressively increases, reaching its maximum in advanced old age. Below are appended three series of age statistics. In the town of Greenock, according to Buchanan, the death rate was as follows:

Age.										Mortality.	
Under 10 years	5.0	per cent.
10 to 20	"	8.6	"
20 " 30	"	15.6	"
30 " 40	"	21.5	"
40 " 50	"	42.0	"
Over 50	"	66.6	"

The death rates of typhus fever in the London Fever Hospital, during a period of two years and including 3506 cases, have been calculated by Murchison as follows:

Age.				Admitted.				Died.	Per cent.
Under	5 years	17	3	17.65
Between	5 and 10 years	183	14	7.65
"	10 " 15	"	363	18	4.95
"	15 " 20	"	546	26	4.76
"	20 " 25	"	495	47	9.05
"	25 " 30	"	343	52	15.15
"	30 " 35	"	323	55	17.02
"	35 " 40	"	270	89	32.96
"	40 " 45	"	292	87	29.79
"	45 " 50	"	212	83	39.15
"	50 " 55	"	150	78	52.00
"	55 " 60	"	100	51	51.00
"	60 " 65	"	88	49	55.68
"	65 " 70	"	42	28	66.66
"	70 " 75	"	24	17	70.83
"	75 " 80	"	6	5	83.33
Over	80 years	2	2	100.00
Age unknown	50	11	22.00
							<u>3506</u>	<u>715</u>	<u>20.89</u>

Guttstadt¹ gives the figures for 5545 cases admitted into Prussian hospitals from 1878 to 1880:

Age.		Males.	Females.
Under	10 years	2.2 per cent.	2.3 per cent.
Between	10 and 15 years	3.0 "	1.5 "
"	15 " 20 "	5.2 "	4.5 "
"	20 " 30 "	8.2 "	10.1 "
"	30 " 40 "	16.0 "	11.2 "
"	40 " 50 "	31.9 "	20.2 "
"	50 " 60 "	43.7 "	25.5 "
Over	60 years	57.1 "	45.2 "

It will be seen that while Guttstadt's tables exhibit lower mortality rates than Murchison's, the same general influence of age is shown.

Curschmann believes that the increasing death rate after the age of forty is due to the greater cardiac weakness at this period and to the increased liability to hypostatic congestion of the lungs and other pulmonary complications as a result thereof.

Sex.—Sex appears to exert but little influence upon mortality. Murchison's figures give 19.67 per cent. of deaths in males and 18.20 per cent. in females.

Hygienic Environment.—The social position and financial condition of individuals influence to a large extent the character of their surroundings. Food, mode of life, and domiciliary environment, by modifying the physical, mental, and moral tone of persons, influence to that extent their general health and resistance to disease, and also their ability to successfully cope with disease when stricken.

The mortality of typhus fever is particularly high among people debilitated by famine and hardship. Physical exhaustion, such as occurs in soldiers and among hard-worked nurses and physicians, doubtless accounts for the comparatively high mortalities among these classes of patients. The overcrowding and unhygienic conditions which often prevail in barracks, prisons, and on board ships increase not only the incidence of typhus, but also its mortality.

Murchison divided the patients admitted into the London Fever Hospital into three classes, according to their social and financial condition:

	Admitted.	Died.	Per cent.
1. Pay patients	94	15	14.89
2. Patients admitted free, but not classified as paupers.	2674	497	18.6
3. Paupers	738	204	27.6

It is seen from these figures that the mortality is higher according to the poverty of the patients. Murchison believes, however, that the larger death rate among the poorer patients is to be explained by the more advanced age of these persons. He states that the current opinion in Ireland is that the disease is accompanied by a higher mortality among the rich than among the poor.

Intemperance and Previous Health of Patient.—It is no less true of typhus fever than of smallpox and other infections that the disease is

¹ Quoted by Curschmann.

particularly fatal in alcoholics. Prolonged habits of intemperance produce structural changes in the heart, bloodvessels, kidneys, liver, and nervous system, and weaken the defensive resources of the body when attacked by disease. In typhus fever, as in smallpox, hemorrhagic attacks are more common in drunkards than in other individuals.

The previous existence of chronic organic diseases or of acute diseases unfavorably influences the prognosis in typhus fever, as would naturally be expected. Debilitating illnesses which lower the resisting power of the individual, or diseases in which the structural integrity of important organs is affected, very considerably lessen the chances of recovery.

Unfavorable Symptoms.—Great intensity of any or all of the symptoms of typhus fever constitutes an unfavorable condition, yet the comparatively brief course of the disease renders it possible for patients exhibiting even the most alarming symptoms to recover.

High fever during the invasive stage and the remaining days of the disease, if unattended by symptoms hereafter to be mentioned, need not be regarded as of specially unfavorable significance. If, however, the temperature continues very high during the second week, it indicates an attack of great gravity.

More important than the temperature is the condition of the heart and the bloodvessels. Licéaga regards an early disproportion between the pulse rate and the temperature as a sign of fatal omen. A pulse rate of over 120 in the beginning of typhus fever should excite solicitude. But the frequency of the pulse is not the only factor to be considered. The rhythm, volume, and compressibility of the arterial pulsations and the character of the cardiac sounds are of equal or greater importance. Inaudibility of the first heart sound or irregularity, rapidity, or marked compressibility of the pulse occurring early in the disease are bad prognostic signs.

The condition of the nervous system offers valuable evidence. Early wild delirium, persistent insomnia, progressively deepening stupor, subsultus tendinum, carphologia, muscular twitchings, and convulsions are all of evil portent. The occurrence of profound coma or coma-vigil renders the prognosis hopeless.

The presence of considerable albumin in the urine during the early days of the disease indicates a grave infection. When blood and casts are associated an alarming complication is present.

Pulmonary complications are commonly the cause of death, particularly in persons advanced in years. Hypostatic congestion, severe and widespread bronchitis, and pneumonia swell the mortality list. Curschmann includes marked meteorism and "pinhole pupils" among the specially unfavorable symptoms.

The profusion of the rash is of less prognostic import than its special characters. The early appearance of petechiæ and an unusual degree of hemorrhagic extravasation into the skin are grave signs. Pronounced cyanosis of the skin, particularly of the face and extremities, indicates cardiac weakness and is, therefore, an ominous manifestation.

Among the *favorable* symptoms are moderate intensity of the fever,

ability to sleep, preservation of the faculties of the mind, moist tongue, moderate frequency of the cardiac pulsations, and early subsidence of the pyrexia.

Mortality Rate.—The death rate of typhus fever varies considerably in different epidemics, but will be found usually to be in the neighborhood of 18 or 20 per cent. Murchison found that the mortality of 4757 cases of typhus fever treated in the London Fever Hospital between 1848 and 1862 amounted to 20.89 per cent. The same author collected the immense number of 18,592 cases treated in London, Glasgow, and other cities, and calculated the mortality as 18.78 per cent. Lebert gives the general mortality in his experience as 15 per cent.; Buchanan, 10 per cent.; and Curschmann, 23.4 per cent.

The mortality in hospitals is higher than in private practice. This may be in part accounted for by the larger percentage of grave and moribund cases received in hospitals.

In the most severe epidemics the mortality may reach 30, 40, or even 50 per cent. During military campaigns and in famine-stricken communities the death rate is apt to be particularly high.

THE TREATMENT OF TYPHUS FEVER.

Prophylaxis.—In the prevention of such a disease as typhus fever two lines of action are to be pursued. It is of paramount importance to limit the infection, as far as possible, to the first afflicted patients. This is to be accomplished through isolation of the sick and disinfection of all articles which have come into contact with the patients. If these measures could be carried out with precision and certainty, little else would be necessary. But epidemics within recent years demonstrate that even with the employment of modern methods it is impossible to completely circumscribe the infection of the disease. It becomes necessary, therefore, to remove all those causes in a community which favor the development and dissemination of typhus. It has already been pointed out that the congregation of large numbers of people in closely crowded and poorly ventilated quarters is a potent contributory cause in the spread of the disease. When the original infection is introduced such conditions offer the most favorable opportunity for the development of an epidemic. In countries in which typhus is prone to appear, the health authorities should prevent the concentration of men in barracks, prisons, lodging houses, tenement houses, and the like. When this cannot be avoided free ventilation of these quarters must be insisted upon.

It is likewise desirable to control, as far as possible, the movements of beggars and vagrants in crowded slum districts; it is an oft-repeated experience that these persons serve as carriers of contagion. Licéaga quotes Monjares as stating that the removal from populous centres of the crowds of beggars who swarmed the streets of San Luis Potosi caused the disappearance of an epidemic of typhus fever which prevailed in that town.

As typhus often follows in the wake of famine and warfare, the most rigid precautionary measures should be employed when these conditions exist. Proper camp sanitation and care as to the feeding and housing of troops are of great importance. This was exemplified in the Crimean War in the relative freedom of the English soldiers as compared with the French. The English army, owing to more stringent hygienic control, suffered much less from typhus fever than did the French troops.

Isolation.—As is true of all contagious diseases, the typhus patient must be separated from other persons during the entire period of his illness. This can be most effectively accomplished by sending him to a hospital specially set apart for the purpose. No one at the present day would hazard placing a typhus patient in the wards of a general hospital.

Where the patient must be treated at his home, an airy room in the upper part of the house should be selected.

Carpets, curtains, and all dispensable furniture should be removed from the apartment. A communicating room should be occupied by the nurse and likewise utilized to disinfect all articles leaving the sick apartment. Over the door communicating with the corridor should be suspended a sheet wet with a 5 per cent. solution of carbolic acid or a 1:1000 solution of bichloride of mercury. Whenever possible the attendants and nurses should be chosen from those who have once passed through an attack of the disease. One attack of typhus fever protects against a second in the vast majority of cases. When an immune nurse cannot be secured, the one employed had better not sleep in the sick-room. Non-immune nurses should not be permitted to go abroad among people, for fear of spreading the disease. Immunes may be permitted this privilege only when every precaution as to personal cleanliness and disinfection is taken. Intercommunication between the patient and members of his family must be strictly prohibited.

Disinfection.—The destruction of the infection in all articles with which the patient has come in contact is a measure of the highest importance. Mention has already been made of the frequent transmission of typhus fever in the body linen of patients. To lessen the intensity of the infection in these articles frequent bathing of typhus patients is desirable. The baths, which may be sponge or plunge baths, subserve the double purpose of reducing temperature and lessening the dissemination of the contagium of the disease.

The body and bed linen should be changed once or twice a day. They should be received into an appropriate receptacle containing a 5 per cent. solution of carbolic acid or a 1:2000 solution of bichloride of mercury.

The bodily excretions should be disinfected with chloride of lime or one of the above-mentioned antiseptics. While there is no convincing proof that the infection of typhus is resident in the dejecta, the disinfection of the stools and urine is a wise and easily carried out precaution. Eating utensils should be thoroughly boiled before being permitted to leave the sick-apartments.

The physician in attendance upon typhus patients should protect his clothing by wearing a long gown and a cap which covers as much of his hair as possible. On leaving the patient he should carefully wash his face and hands and air himself thoroughly before seeing another patient.

After the recovery of the typhus patient the apartments occupied should be thoroughly fumigated with formaldehyde or sulphur and subsequently aired for a number of days before occupancy. Walls should be whitewashed, painted, or repapered according to desire. Blankets and mattresses should be subjected to superheated steam or hot air in the disinfecting plant provided by most large cities. When such facilities are not available, blankets should be boiled and mattresses burned and destroyed.

Wooden furniture should be washed with a solution of carbolic acid or bichloride of mercury. The patients' clothing should be disinfected by formaldehyde, steam, or hot air.

When death occurs the body should be enveloped in a sheet saturated with a carbolic acid or corrosive sublimate solution. An hermetically sealed casket should be used and interment should be private.

Ventilation.—Ventilation is a preventive measure which appears to be of greater value in typhus than in other disease. That the free admixture and circulation of fresh air in the sick-apartment or ward lessens the danger of contagion is admitted by all writers. Lebert says he found it an excellent plan, even during the severest cold of winter, to keep the windows open part of the day and night; he adds that the patients bear cold well during the continuance of fever, but are sensitive to it later.

When epidemics occur in the summer months it is a good plan to treat the patients in tents. The liability of attendants contracting the disease under these conditions is distinctly lessened.

The temperature of the sick-apartments should be in the neighborhood of 65° F. The floor is to be mopped with an antiseptic solution and the atmosphere kept free from dust.

Nursing.—The nursing of typhus fever is of great importance and requires the services of a trained person. The body surface should be frequently sponged with water containing a little alcohol or with a weak carbolized solution. The teeth and oral cavity require careful attention from the beginning; mild antiseptic mouth washes should be employed. Diluted Dobell's solution, boric acid water, or a diluted peroxide of hydrogen may be used. The cleansing of the mouth is of particular importance when the patient is stuporous, as the mucous membrane becomes dry and covered with mucus and blood crusts.

Careful attention is necessary to prevent the development of bed-sores. Frequent ablutions of parts subjected to pressure and soiled by excretions, and the use of pads or pneumatic cushions to relieve pressure, will accomplish the object desired.

Diet.—The diet is the same as that prescribed in the other acute exanthemata. During the intense febrile period the patient will desire

nothing but liquid nourishment. Milk and broths may be given every two or three hours. As soon as the patient cares for soft foods he may be allowed to have soft-boiled eggs, gelatin, gruels, milk-toast, and like foods. As the disease abates and the appetite increases, a gradual return to the usual dietary may be begun. For the relief of thirst lemonade and the carbonated waters may be given. The diet need not be as rigid as in typhoid fever, in which disease the presence of intestinal ulceration necessitates great caution.

Medical Treatment.—Although numerous remedies have been advocated from time to time for their beneficial action upon typhus fever, it must be admitted that we know of no drug which materially affects the course of the disease. When the specific cause of typhus is discovered a specific cure for the disease may be forthcoming. The most approved treatment of typhus is that which is devoted to an alleviation of the symptoms and the maintenance of the patient's strength.

Fever.—The fever in typhus often reaches a great height and calls for measures to reduce its intensity. Almost exclusive reliance is to be placed upon hydrotherapy in one form or another. In the milder cases it may suffice to employ tepid sponge baths several times a day. The application of an ice-bag or Leiter's coil to the head is a useful supplementary measure. When sponge baths are not sufficient to control the pyrexia recourse may be had to the wet pack, the sheet being wrung out of tepid or cold water according to the intensity of the fever. The continuous tepid or warm bath will be found to control the temperature in a most satisfactory manner; the patient may be kept for twenty-four hours or longer in a bath the temperature of which is maintained between 93° and 98° F. When the graduated bath is employed the water is at first warm, but is gradually lowered by the addition of cold water to 75° or 70° F.

The Brand method of cold bathing so extensively adopted in the treatment of typhoid fever does not seem to have been systematically tried in typhus fever, although its main features are referred to in favorable terms by those experienced in the treatment of typhus. With one or other of the above hydrotherapeutic measures it will be found possible to control excessive fever. It should be remembered that the reduction of fever by these measures is merely one of the objects desired. Baths exert a tonic influence upon the respiratory and circulatory centres and allay nervous excitability.

The coal-tar antipyretics should not be used except in very moderate doses. When given in large doses or over a long period of time they may produce serious cardiac depression. Phenacetin, antipyrin, and lactophenin are among the most eligible of these preparations.

Nervous Symptoms.—HEADACHE is commonly so persistent and distressing as to require remedies for relief. The light in the room should be kept subdued in order to lessen retinal irritation. An ice-bag should be applied to the head, and bromide of sodium, phenacetin, or antipyrin administered. When these remedies fail to control the cephalalgia it may be necessary to give opium.

INSOMNIA.—Inability to sleep is a bitter complaint of typhus patients during the early days of the disease. It is well to first try the bromide of sodium in 20-grain doses, repeated once or twice during the night.

In other cases chloral appears to do well, but should not be used in large doses for fear of depressing the heart. Ten grains may be administered in the evening, and followed later by a 15-grain dose if necessary. Where sleep cannot be otherwise obtained it is proper to give a hypodermic injection of morphine. The employment of a warm or tepid bath at the sleeping hour will often materially aid in quieting nervous excitement and inducing sleep.

DELIRIUM.—The bromides, chloral, and opium may be employed to quiet excessive cerebral activity. The best result in many cases is obtained by an ice-bag to the head and a prolonged warm bath, or, when the temperature is very high, a cold bath or pack.

Constipation.—In the constipation which usually exists early in the disease calomel in fractional doses may be given or a mild saline may be used. One of the disadvantages of employing opium in typhus is the aggravation of the existing constipation. When there is much fever a cold, high enema will serve a double purpose. Vomiting, when present, may be controlled by pellets of ice, carbonated or lime water, and temporary abstention from food. The late diarrhoea is best checked by bismuth internally, and starch-water and laudanum enemata. Meteorism may, when mild, be relieved by laxatives, and turpentine internally and externally. Severe gaseous distention occurring late is a grave symptom, often defying all treatment.

Alcohol.—Alcohol is a remedy of great value in the treatment of typhus, when it is used with discrimination. It should not be employed as a routine, but rather to combat special symptoms. Many patients will not require its use at all. Buchanan says that alcohol is needed in two classes of patients—those who cannot take a sufficient quantity of nourishment, and those habituated to the use of stimulants. He enumerates the special indications as follows: Alcoholic stimulants are most serviceable in (1) old people; (2) in cases of great prostration with low delirium and coma; (3) where the pulse is very compressible and the first heart sound feeble; also when the pulse is rapid or irregular; (4) where the extremities are cold and the surface livid; (5) where there is much congestion of the lungs; (6) where there is any erysipelatous complication.

It may be given in the form of whiskey, brandy, or wine, or, as Curschmann prefers, in Stokes' cognac mixture, the formula of which is as follows:

R \bar{c} —Cognac opt.,	
Aqua dest	℥i 15 ounces.
Vitell ovl	No. 1.
Syrup	6 ounces.

Tablespoonful every two or three hours.

When the *pulse* becomes compressible, rapid, or irregular, or when the first heart sound is weak, it may be necessary to resort to other cardiac stimulants in addition to alcohol. Strychnine, digitalis, stro-

phanthus and caffeine may be employed with advantage. Nitroglycerin and camphor dissolved in olive oil may be used hypodermically to tide over critical moments.

Pulmonary and renal complications are to be treated in the same manner as when these conditions arise independently.

In conclusion a word of caution should be uttered concerning the necessity for constant vigilance on the part of the nurses and attendants to prevent suicidal or homicidal attempts during maniacal excitement.

CHAPTER XII.

DIPHTHERIA.

Definition.—Diphtheria is an acute infectious disease characterized by the production of a fibrinous exudate or false membrane on certain parts of the mucous surface of the body. The regions by far most commonly involved are the tonsils, the pillars of the fauces, the soft palate, the uvula, the pharynx, and the nares. Not infrequently the disease extends into the larynx; or it may begin there primarily and remain limited to this locality. Except at the onset, or when there is laryngeal involvement, febrile reaction is not a prominent symptom.

The disease is caused by a specific micro-organism and begins as a local affection, but becomes systemic as the result of absorption of toxins elaborated by the specific bacilli and, perhaps, certain associated bacteria. In severe cases the toxæmia may be extreme. After the general symptoms have disappeared, paralysis is liable to follow. This may be limited to a few muscles, or there may be complete ataxia.

History.—Of the various diseases belonging to the infectious group, which have prevailed from time to time in epidemic form, diphtheria is believed to be one of the oldest. Some writers have sought to prove that it was known at the time of Hippocrates, and described under the name of *Malum Ægyptiacum*. While in the absence of sufficient literature on the subject this cannot be determined definitely, yet it is true that Aretæus, a Greek physician of Cappadocia, who lived in the latter part of the first and the beginning of the second century, portrayed the critical features of this malady in language which warrants the belief that the disease he described was diphtheria. He speaks of a thick, white, moist material which forms over the tonsils and spreads over other parts of the mouth; of ulcers which appear on the tonsils, and which may be superficial and benignant, or extensive, putrid, and malignant, according as the case is mild or severe. In malignant cases the fœtor from the mouth is loathsome. Fluids are sometimes regurgitated through the nose in the effort of swallowing, the voice is husky, and when the disease extends into the air passages death speedily results from suffocation. He mentions that the disease is most common among children. Aretæus believes that this malady originated in Egypt, Syria, and especially in Coele Syria; hence the name of *Malum Ægyptiacum*. It was also known by the name of Egyptian and Syrian Ulcerations.

During the fourth century a disease presenting the same symptoms prevailed in epidemic form in Rome, and was described by Macrobius. From this time forward for several centuries there seems to be a paucity of literature upon the subject; this may possibly mean that there was a long lapse of epidemic prevalence of the disease.

In the sixteenth, seventeenth, and eighteenth centuries epidemics of a disease presenting the essential characteristics of diphtheria are said to have prevailed frequently, and often with great virulence in many parts of Europe, particularly in Holland, Spain, Italy, France, and Germany. The affection appeared also in England, and was described by Fothergill, Huxham, and others. In Spain the disease was known by the name of *fregar* when confined to the fauces or the cavity of the mouth, but when it appeared in the larynx and caused suffocation it was called *garotillo*. In the different countries in which the disease appeared it was described by the physicians under various names, such as, besides those already mentioned, cynanche maligna, cynanche contagiosa, angina maligna, angina gangrænosa, ulcerative sore throat, malignant sore throat, morbus suffocans vel strangulatorius, epidemic croup, etc.

It is not known exactly when this malady made its appearance in America. In 1771, Samuel Bard, of New York, published a brochure entitled, "*An Enquiry into the Nature, Cause, and Cure of the Angina Suffocativa, or Sore Throat Distemper*, as it is commonly called by the inhabitants of this City and Colony." In this article a clinical description is given of a disease comparable in its essential features to diphtheria. It prevailed chiefly among children under ten years, and was evidently infectious. Bard says the disease began as a sore throat, which, upon examination, showed that the tonsils were swollen and inflamed, and presented a few white specks which, in some cases, increased so as to cover the entire surface of the tonsils "with one general slough." The swelling was sometimes so great as to interfere with deglutition. In other cases there was difficulty of breathing, which was often of so great a degree as to threaten immediate suffocation. In his brochure Bard speaks of an article previously written by Douglass, of Boston, describing a new epidemic of an acute throat affection which was seen in that city, and which was quite similar in its clinical manifestations to the disease which later appeared in New York City.

It must be said that these clinical descriptions by the earlier writers were not very exact, and that doubtless several diseases were not infrequently included in the same category. It is safe to assume that some of the anginose affections other than diphtheria, especially scarlatina, were not always differentiated. Indeed, Bard speaks of "inflamed and watery eyes, a bloated and livid countenance, with a few red eruptions here and there upon the face," as being among the earlier symptoms in many of the cases that came under his observation. Likewise, Douglass characterized the disease he described as "An Eruptive Miliary Fever, with Angina Ulcusculosia."

In regard to the history of diphtheria in America, literature shows that the peculiar form of sore throat described by Douglass was seen about 1735 in certain inland towns in New England, and gradually spread westward, reaching the locality of the Hudson River two years later. The disease prevailed more particularly in towns to which people

resorted for trade, and was spread by means of commercial intercourse and travel. In New York an epidemic was noted by Father Middleton in 1752. After Bard's description of the disease in 1771 very little seems to have been said about its presence in New York until 1826. From 1855 to 1858 it prevailed in some parts of the State, especially in Albany, with great malignancy.

In 1856 Dr. J. V. Fourgeand published a monograph on a terrible epidemic of sore throat which occurred in San Francisco and other towns of California.

An epidemic of a similar affection occurred in Philadelphia as early as 1809. Again in 1831 another epidemic prevailed. The records of the Health Office of Philadelphia, however, do not show that any deaths occurred in this city from "diphtheria" until 1860, during which year the number reached 307. From the preceding historical facts it is quite evident that diphtheria was not a newly imported disease in Philadelphia in 1860, but that it previously prevailed under other names.

The earliest accurate observations on the clinical manifestations of diphtheria were made by Bretonneau, of Tours, in 1821, when he presented his first celebrated paper on the subject to the French Académie de Médecine. This paper, it is said, was not published until 1826. The name he suggested for the disease was *Le Diphthérite*, or Diphtheritis. He gave it this name because of its essential characteristic, namely, the formation of a false membrane. Subsequently the name diphtheria was proposed by Trousseau. This title, as Flint suggests, has the negative merit of not involving any hypothesis as to the pathology of the affection. Bretonneau, however, believed that the membranous exudate itself constituted the pathological criterion for the disease; that an inflammation without an exudation is not a diphtheritis, neither is an inflammation with an exudation when it is not infectious. In other words, he not only regarded the exudate as an essential part of the disease, but also as constituting the only source of the infection. He believed the contagium spread, not through the atmosphere, but by inoculation, as it were, resulting from particles of the exudate, either in a fluid or dust-like state, coming in immediate contact with the moist mucous membrane.

Bretonneau's observations, which were quite extensive, led him to conclude that membranous croup and diphtheria were identical affections; the only difference being that in croup the disease process extended into the larynx and trachea. He at first fell into the error of regarding diphtheria as wholly a local disease, but later frankly admitted that systemic poisoning was an essential pathological condition. Angina gangrænosa, he declared, is in no way related to this affection.

Trousseau with his acute power of clinical observation directed attention to the difference between diphtheria and some of the throat affections, especially scarlatina, with which it was often confounded, and also pointed out the danger of this disease from its liability to extend into the air passages. The fact that death not infrequently resulted

at an early period of the disease from an adynamic condition was observed by him and especially commented upon. He is credited with rendering valuable assistance to Bretonneau in establishing the operation of tracheotomy for the relief of membranous croup; even the indications given by him for its adoption would still serve as a useful guide for us at the present day.

Recognizing that the disease was primarily local, Bouchut recommended the removal of hypertrophied tonsils when covered with an exudate, with the object of preventing the membrane from extending downward into the larynx and trachea. He was the first to practise "tubage" of the larynx for relief of the stenosis caused by membranous croup.

This procedure, however, was condemned and fell into disuse for nearly a quarter of a century, when, in 1880, it was revived and brought to a high state of perfection by O'Dwyer, of New York. Intubation is now almost universally regarded as an indispensable auxiliary in the treatment of membranous croup.

After Bretonneau's publication appeared diphtheria was recognized and described by the physicians of every civilized country, and there soon developed a wealth of literature upon the subject. Many excellent works were published by French, German, and English writers. There were, however, some conflicting notions regarding the nature of the disease. Some maintained that it began as a general systemic infection, entirely independent of any previously existing local affection. In other words, the exudate was regarded as a local expression of a constitutional disease, manifesting itself by preference upon the mucous membrane of the fauces, just as the rash of scarlet fever does upon the skin. This view was opposed by most of the ablest writers, and in the light of our present knowledge is regarded as untenable.

The question about which there was perhaps the greatest difference of opinion was whether diphtheria and membranous croup were identical affections, or whether they constituted two distinct morbid processes. It may truly be said that physicians of the present day are not yet entirely agreed on this question. Bretonneau, Wagner, and many others contended that no clinical or pathological distinction between these diseases could be made, while Virchow threw the weight of his authority on the opposite side of the question. This distinguished pathologist sought to establish an anatomopathological distinction. He believed he had succeeded in showing that in the croupous form of inflammation the exudation is deposited upon the surface of a sound mucosa, while in diphtheritic inflammation the exudation takes place into the very substance of the mucosa as well as upon its surface, and that this membrane undergoes interstitial necrosis from want of nourishment caused by compression of the bloodvessels. This attempt to distinguish between membranous croup and diphtheria has been unsuccessful, and the leading clinicians and pathologists now admit their specific identity.

The consideration of diphtheria has assumed a new phase since bacteriology has become so important a hand-maiden to the clinician.

The study of micro-organisms in their relation to this disease dates back over a period of many years, even more than a quarter of a century. In 1868, Oertel, together with Buhl and Hueter, discovered bacteria in the false membrane, the blood, and in certain tissues of patients, which he believed sustained a causal relation to the disease. He described these organisms as presenting various forms, such as spherical, rod-like, and corkscrew-shaped. They were also demonstrated by von Recklinghausen, Nassiloff, Waldeyer, Klebs, Eberth, Heiberg, and others. While these investigators were evidently working along the right lines, and may have seen the specific bacillus, yet they failed to differentiate it from its associates.

The credit of discovering the true bacillus of diphtheria belongs to Klebs, of Zurich. It is generally stated that this discovery was made in 1883, but Lennox Browne makes the following statement in reference thereto: "Professors Hamilton and Sternberg have drawn attention to its discovery by the same observer (Klebs), and to publication of the fact at a congress held at Wiesbaden so far back as the year 1875. The circumstance appears to have attracted but little attention, notwithstanding that on examination of the original reference it is found that Klebs had announced at this date that he had not only detected the bacillus, but that he had also made an effort to cultivate it, and, as far as one can judge, successfully. To Klebs, therefore, the credit of having discovered this organism is undoubtedly due. But since he never definitely announced that he had been able to obtain pure cultures of it, it must be said that he failed in establishing its causal relationship to the disease."

This relationship was later established in 1884 by Loeffler, who succeeded not only in obtaining pure cultures of the bacillus, but also in proving its specific character by communicating diphtheria to guinea-pigs and birds by inoculating them with this organism. Hence, through the combined labor of these two investigators, in discovering and establishing the specificity of this micro-organism, it is known by the name of Klebs-Loeffler bacillus. This discovery has had the effect of settling the long and often animated controversy as to whether diphtheria is primarily a constitutional or local affection in favor of the latter, and has placed the study of the disease on a scientific basis.

THE ETIOLOGY OF DIPHTHERIA.

In considering the causation of diphtheria in the light of our present knowledge it might be thought sufficient to give simply a description of the Klebs-Loeffler bacilli and the associated bacteria, with an explanation of their causative relation to the local and systemic manifestations of the disease. This is the course pursued by many writers of the present day. But while it is impossible to convey a correct knowledge of the etiology of diphtheria without carefully describing its bacteriology, yet for a comprehensive understanding of the subject it is necessary also to consider the predisposing causes as well as the means

by which the disease may be disseminated, and the conditions favorable for its spread.

The disease is contagious. While sporadic cases may be met with, yet when it once obtains a foothold in a community it is particularly prone to assume an epidemic character. The evidence of its infectiousness is very conclusive. When diphtheria appears in a family it frequently attacks many members in succession. The fact that some members of the family often escape is no evidence that it is not contagious, for this not infrequently happens with scarlet fever, the contagiousness of which no one doubts. In regard to such instances it may be said that ever so little positive evidence outweighs any number of negative facts. Further evidence of its contagious nature is found in the fact that physicians and nurses in attendance upon cases very frequently contract the disease. In the Municipal Hospital of Philadelphia most of the resident physicians who have worked in the diphtheria wards have suffered from the disease in variable degrees of severity. In one instance the attack was so severe that death resulted at an early stage. The majority of the nurses have shown symptoms more or less marked soon after beginning work in the wards. It is not unusual for physicians and nurses who have been in attendance upon cases in private practice to be admitted to the hospital suffering from the disease.

Not infrequently diphtheria has been communicated by direct contact with detached pieces of exudate or the secretions from the throat and nose of patients. We have known nurses to show symptoms of the disease within forty-eight hours after having had coughed into their faces some of the infectious material from the throats of patients. We have likewise known infection to result from kissing. More than one physician has fallen a victim to diphtheria through his zealous efforts to save the life of a patient by clearing out an obstructed tube after tracheotomy by suction, or by trying to inflate the lungs after the operation by blowing his own breath into them through a tube. Oertel says: "In this way Otto Weber, Seehusen, Valleux, Blache, Cillite, fell sacrifices to their professional devotion. Dr. Wiessbauer, of Munich, lost his child, who had a short time previous to its death unfortunately gotten hold of a cannula and put it in its mouth, the cannula having just been removed from a patient sick with diphtheria." Still further evidence that the disease is infectious is found in the fact that it has been communicated to some of the lower animals experimentally by inoculation.

It is well known that diphtheria, like all contagious diseases, sometimes occurs sporadically, at other times endemically, and then again epidemically. In attempting to explain these circumstances one must take into consideration not alone the *causa causans*, or the specific germ of the malady, but also the *causa efficiens*, or that which determines the occurrence of widespread epidemics. In studying the latter it is necessary to enquire into the sanitary surroundings of each particular locality where the disease prevails, and into all conditions which may influence individual receptivity to the infection, such as climate, domestic environment, age, sex, rainfall, season, etc.

Geographical Distribution.—No country can be said to be absolutely exempt from diphtheria, although it prevails to a much greater extent in some places than in others. The disease has invaded both hemispheres, and it has occurred in the northern and southern portions of each. Altitude seems to exert but little influence over its spread, as it has been found in both high and low-lying countries. According to statistics of the United States, however, it has caused the greatest proportion of deaths in the Southern Central Appalachian region, the Central Appalachian region, and the region of the Western plains; while the proportion of deaths was least in the South Atlantic coast region and the Gulf coast region.

The disease occurs in the higher degrees of latitude; but of all localities it is most common in the temperate zone and that part of the frigid zone immediately adjacent thereto, and least common in the tropics. The records of India show that it is rare in the tropical climate of that country; nor does it thrive anywhere in the tropical parts of Asia. It is also rare in Central and South America.

Conditions of the Soil.—Some writers have ascribed to the soil a certain influence over the propagation of the disease. It was a common impression among the older writers, and, indeed, some of the more modern still hold to the opinion, that low, damp soil, such as is found in marshy regions with bad drainage, especially near rivers which frequently overflow their banks and where there is a good deal of vegetable matter undergoing decomposition, favors the development of diphtheria; while, on the other hand, a high, dry soil, or a soil composed largely of dry sand has been regarded as unfavorable to the spread of the disease. At least, some observers claim that it appears less frequently and is less likely to be disseminated in localities characterized by the latter geological conditions.

While it is recognized that for the production and propagation of diphtheria the presence of the specific micro-organism must be regarded as a *sine qua non*, yet it is not improbable that these organisms may thrive under certain conditions and perish under others. Whether soil in any of its forms exerts any such influence one way or the other is uncertain. At times it does appear as though such an influence was especially marked, yet statistics show that the disease has occurred and even prevailed in epidemic form in districts where the local conditions were regarded as unfavorable for its spread.

According to Lennox Browne, epidemics of diphtheria in England "have been very catholic in their distribution from both the geographical and the geological aspect." But an interesting table compiled by him seems to justify the belief that the disease has a decided preference for a clayey soil. This table bears out the opinion of Dr. Thorne Thorne, whom he quotes as saying that "where a surface soil is, by reason of its physical constitution and topographical relations, such as to facilitate the retention of moisture and of organic refuse, and where a site of this character is, in addition, exposed to the influence of cold and wet winds, there you have conditions which tend to the fostering and fatality of

diphtheria, and also go to determine the specific quality of local sore throat." The marked predilection of the disease for wet, clayey soils has been commented upon by many writers, some of whom have pointed out that diphtheria is not only more common but more fatal in localities with wet and retentive soils than in those with dry and pervious ground conditions.

Evidence could be cited tending to show that the disease is fostered by decomposing heaps of manure and vegetable refuse, such as are found about stables where sheep, cattle, and other animals are kept. Outbreaks of diphtheria have been reported where this condition existed in close proximity to dwelling-houses. The drainage from decomposing animal and vegetable matter imparts to the soil a serious contamination. The digging up of old drains, especially those connected with dwelling-houses, has been followed more than once by an outbreak of diphtheria. Surely the upturning of soil thus polluted is a fertile source of diphtheroid sore throats, or pseudodiphtheria, if not of the true disease itself. At any rate it cannot be denied that the emanations from such a source act as a predisposing cause to precipitate an attack when the diphtherial entity is present.

Rainfall.—The question as to whether the annual amount of rainfall exerts any influence over the prevalence of diphtheria or its mortality has not been positively determined. Statistics have been cited to prove both the positive and negative sides of the question, and are, therefore, conflicting. After fully considering the evidence at hand we are inclined to believe with most writers that rainfall is not a very important factor in determining the diffusion of the disease.

Season.—Diphtheria is undoubtedly much more prevalent during the cold-weather months than during the summer. This is shown very clearly by the statistics of all countries where the disease prevails, and is made especially clear in the last census report on vital statistics of the United States. While the returns of deaths in this report are, for obvious reasons, incomplete, yet they are sufficiently complete for comparative purposes. Of course, the number of cases of diphtheria is not given, but the number of deaths by months may be regarded as a fair index of the prevalence of the disease for the same periods.

The following table shows for the United States the deaths by months from diphtheria in the census year 1900:

Months.	Deaths.	Months.	Deaths.
January	1846	July	827
February	1496	August	898
March	1411	September	1303
April	1156	October	1739
May	1081	November	1912
June	795	December	1904

This table indicates that diphtheria (including croup) is most prevalent in the United States during the nine months beginning with September and ending with May, and least prevalent during the summer months of June, July, and August. The three months showing the greatest number of deaths are November, December, and January.

By dividing the year into quarters, representing the four seasons, we find the number of deaths for each season to be as follows: spring, 3648; summer, 2510; autumn, 4954; winter, 5246. The winter months, and especially the autumn and winter months, show by far the greatest proportion of deaths.

The following table shows the admissions by months of diphtheria patients into the Municipal Hospital of Philadelphia during the last decade:

Year.	Jan.	Feb.	Mar	April	May	June	July	Aug	Sept.	Oct.	Nov	Dec
1893	86	24	21	7	16	24	7	13	5	21	38	17
1894	15	20	33	20	28	25	39	23	30	70	81	60
1895	65	68	66	46	66	54	60	61	38	48	66	73
1896	12	54	67	44	74	60	44	45	60	58	122	141
1897	107	97	76	87	61	100	109	112	87	145	149	130
1898	137	78	71	84	88	78	76	84	121	146	146	128
1899	117	72	81	89	100	103	94	120	110	123	179	164
1900	143	126	119	95	102	102	92	94	108	123	141	112
1901	101	87	98	97	80	76	47	53	66	62	78	60
1902	89	59	59	45	61	55	■	25	38	52	48	45
Total . . .	872	681	691	612	665	677	611	639	676	826	1008	890

This table also shows that the disease was most prevalent during the months of November, December, and January, and least prevalent during the three summer months. Considering the table as a whole, the total number of cases in each of the four seasons is as follows: spring, 1968; summer, 1937; autumn, 2560; winter, 3513.

It will be noticed here that the autumn and winter months furnished by far the largest number of cases. This is in accordance with the observation of many writers. Newsholme says: "Diphtheria is most prevalent in autumn and in the early winter months, when the optimum temperature and the optimum degree of humidity of the soil are rapidly disappearing or have departed. It is also most prevalent after the wet weather, occurring in or immediately following exceptionally dry years. Both these conditions tend to raise the ground water and to drive out any pathogenic micro-organisms from the soil."

The greater prevalence of diphtheria during the cold-weather months can be rationally explained, we believe, by the well-known observations that the fauces and upper air passages are then much more liable to attacks of catarrhal inflammation, thus affording an increased susceptibility to the disease, and that the sanitary surroundings in schools and dwelling-houses at this time of the year are apt to be at their worst.

Domestic Environment.—Under this head might be included the unsanitary conditions of domestic life, such as result from the crowding together of a large number of people into tenement houses, narrow streets, courts, and alleys, where, besides the crowding, the drainage is bad, and the air almost necessarily impregnated with animal emanations and all kinds of foul odors. Surroundings of this nature are sure to prejudice health and exert a definite influence in determining an outbreak of diphtheria and favoring its spread. It is a matter of common

observation in all large cities where this disease is endemic that the inhabitants of such localities suffer to the greatest extent. While persons who live under more favorable circumstances are not spared, yet the transmission of the infection is particularly favored by poverty and uncleanness.

Not alone do overcrowded conditions of dwelling-houses favor the propagation of diphtheria, but in all congested institutions, especially those for the care of children, in factories, schools, barracks, and, in short, wherever there is a large aggregation of persons living under unhygienic environments, there the disease is wont to break out and assume an epidemic form. But, as already stated, more favorable modes of living do not ensure safety against the ravages of the malady. Oertel very truly says: "Robust children who enjoy the best of care and nourishment are seized and carried off by the disease, although the number of such cases does not reach that attained in other classes, in which poverty and uncleanness favor the spreading of the pestilence." Even the rich and cultivated dwellings, under the most modern sanitary improvements of ventilation, plumbing, drainage, and the like, have furnished a fair quota of victims to this fell destroyer of human life. This shows that the specific organism of diphtheria is no respecter of persons; nevertheless, certain environments or conditions of life exert a very potent influence over the spread of the disease.

Dissemination of the Infection.—The infection of diphtheria is commonly communicated through direct exposure to a person suffering from the disease. The dust from a sick-room, contaminated with particles of dried secretions from the throat and nose of a patient, may serve to convey the infection for a short distance through the agency of the atmosphere. The well members of a family in which the disease exists often unwittingly carry the contagium to others. It is frequently disseminated, especially where no attention is given to disinfection, by means of infected articles, such as clothing, bedding, towels, handkerchiefs, carpets, drapery, upholstery, books, toys, and the like. It must be admitted that physicians and nurses are sometimes the agencies of transmitting the infection. Even pet animals may play a part in this baneful work.

Doubtless the disease is often spread by exceedingly mild cases—so mild, indeed, that the symptoms are not correctly interpreted. Of course no restrictions are placed on the movements of persons thus mildly afflicted. Adults continue at their daily vocation, and children go to school as usual. Such cases are constantly met with, especially in large cities where diphtheria is endemic. It is well known that some cases of chronic rhinitis are really of a diphtheritic nature, inasmuch as the Klebs-Loeffler bacilli are sometimes found in this disease. When this condition exists, it is frequently not recognized, and therefore no restrictions are enforced, nor even any precautionary measures advised. Really, it is a question whether the mild and unrecognized cases of diphtheria are not much more often responsible for the spread of the disease than the severe cases, for the latter are usually surrounded with

the proper sanitary measures, such as isolation, disinfection, and the like. Yet it should not be overlooked that after recovery from a well-marked attack patients not infrequently leave their homes and associate with the public before their throats are free from the bacilli. Experience shows that these organisms sometimes remain in the nose and throat in a virulent form for five or six weeks, and at times much longer, after the clinical symptoms have disappeared. Then again, it is not impossible for the disease to be spread by well persons in whose throats the bacilli are present. It has been estimated, by an able observer, that these organisms may be found in the throats of about 2 per cent. of all well persons.

Milk has been charged with spreading diphtheria. In order that it should play this role the infection must be introduced through outside contamination. Once introduced, bacilli will find in milk a good culture medium in which to grow and multiply. In the reports of the majority of epidemics which were believed to have been caused by the milk supply, it is stated that either diphtheria prevailed at the dairies or the milk cans were washed with contaminated water. In some instances it is said the cows showed on their teats and udders inflammatory conditions.

After carefully studying a number of reports on epidemics alleged to have originated from infected milk, we feel obliged to say that the contention is supported only by very strong presumption that the milk was at fault. There is no evidence that amounts to absolute proof. So far as we know the Klebs-Loeffler bacilli have never been found in any of the suspected milk. A few years ago the Board of Health of Philadelphia collected samples of milk from sixty-two houses in which diphtheria prevailed and subjected them to careful bacteriological examination, but the result in every instance was negative. In this connection it might be well to add, on the authority of Lennox Browne, "that the bacillus when grown in milk loses many of its chief characteristics, or, perhaps, it would be more correct to say it assumes others peculiar to its culture medium. It probably undergoes degenerative changes with rapidity; possibly these are due to the presence of lactic acid."

Schools are commonly regarded as an important factor in the spread of diphtheria. It is a matter of observation in large cities where the disease is constantly present that the number of cases increases soon after the opening of the schools in autumn, and that the number is smallest during the summer vacation. The rules created and enforced by health authorities, excluding from school all children suffering from sore throats, and all those from families in which diphtheria exists, have done much to limit the spread of the disease. But in spite of this wise sanitary measure it not infrequently happens that children attend school while suffering from mild and unrecognized forms of diphtheria, or, at least, in whose throats virulent bacilli are present. Outbreaks of the disease in certain districts may often be explained in this way.

On the contrary, efforts have been made to show that congregation in

schools is not a common cause of epidemics. In support of this negative view it has been pointed out that the mortality from diphtheria is by far the greatest among children under five years, who have not yet arrived at the school age. It has been stated also that there frequently is a great increase of its prevalence in schools immediately after a holiday recess. The latter statement is undoubtedly true of boarding schools and kindred institutions; but when diphtheria breaks out in such a school it is apt to cause not only a local epidemic, but so great alarm among the pupils as to occasion a stampede, and thus the disease is often widely disseminated. When the infection is introduced into a family it is not surprising that the younger children—those who have not yet attained to the school age—should be the principal sufferers. Therefore, the fact that the greatest mortality is found to be among children under five years does not invalidate the view that schools operate as an important factor in spreading diphtheria.

While writing these lines a late issue of *American Medicine* comes to hand containing this paragraph: "Diphtheria of a somewhat malignant type is reported to be raging in Milton, Mass. The disease first appeared among the pupils of one of the public schools, and afterward spread to such an extent that the school was ordered to be closed. At this time there were 28 cases in the immediate neighborhood."

Like all infectious diseases, diphtheria is most rapidly disseminated in countries and localities where there is the freest personal intercommunication. Hence, it is by far more common in urban than in rural communities. After having illustrated this fact in diagrammatic form, Newsholme says: "The whole of Michigan, which has a large proportion of rural population, has much less diphtheria than the neighboring city of Chicago; the whole of Massachusetts has less diphtheria than Boston or New York; the whole of England less than London; the whole of Japan less than its great towns; the whole of South Australia less than Adelaide."

Constitutional Predisposition.—The presence of catarrhal affections of the mucous membrane of the nose and throat seems to increase the liability to diphtherial infection. Children who suffer from adenoid growths in the pharynx, with chronic inflammation of the nasopharyngeal region, and from enlargement of the tonsils are regarded as being particularly susceptible to the infection. When these conditions exist together they usually cause what is known as mouth-breathing, by which act the air, instead of being warmed and filtered by passing through the nares, goes direct to the fauces cold and irritating, and, perhaps, laden with germs. Lennox Browne writes: "My personal experience leads me to say that diphtheria hardly ever, if ever, occurs in a child under seven years of age who is not the subject of one or other of these forms of glandular overgrowth. It appears needless to enforce their tendency to abrogate the hygienic function of the nose as the first avenue of respiration and to induce the marked deficiency in vitality and resisting power to contagion which are to be found in all such children."

Everyone knows that the first evidence of diphtheria is commonly seen on the tonsils. It would, therefore, appear that these glandular organs were the most vulnerable part of the body for attack by the Klebs-Loeffler bacilli. The peculiar anatomical structure of the tonsils, having on their exposed surface deep crypts or lacunæ into which the organisms may lodge and multiply, affords a very probable explanation why they are so often the seat of the disease process. When these glands are inflamed and swollen the lacunæ become deeper and the mucous covering so delicate that they have been not inaptly compared by Virchow to open wounds. Hence, it is easy to see how this condition may increase susceptibility to diphtheria.

Certain other diseases with anginose manifestations also furnish a marked predisposition to diphtheria. Of these we would mention particularly *scarlet fever* and *measles*. The frequency with which the Klebs-Loeffler bacilli are found in the throats of scarlet-fever patients is really astonishing; according to our experience at the Municipal Hospital they are present in 10 per cent. to 33 per cent. of all cases. Indeed, they are often found when the clinical conditions would not suggest the existence of diphtheria. These two diseases, however, not infrequently coexist, the symptoms peculiar to each appearing at the same time. But symptoms of diphtheria may develop during the course of scarlet fever or during convalescence.

As might be expected from what has already been said, the catarrhal affection of the fauces and upper air passage incident to measles renders the individual very responsive to the action of the diphtheria bacillus. Membranous croup associated with measles is by no means an infrequent occurrence, and, moreover, is exceedingly fatal. When measles prevails in Philadelphia we have numerous applications for the admission to the Municipal Hospital of cases complicated with membranous laryngitis. Many of them belong to the true type of diphtheria, but others, it must be admitted, are probably caused by other bacteria, as the diphtheria organism is not always found.

The predisposition to diphtheria varies greatly in different persons, and often quite independently of any known abnormal condition of the throat. Children are much more susceptible than adults. The predisposition is undoubtedly much more strongly marked in some families than in others. This may be explained on the supposition that in the more susceptible families there is an inherited tendency to the development of some form of chronic catarrh of the mucous membrane of the throat, thus favoring the operations of the bacilli. Some writers believe that infection through a healthy mucous membrane, if not impossible, is very unlikely.

Recurrent Attacks.—In most infectious diseases one attack usually confers immunity against subsequent attacks. This is particularly true of measles, scarlet fever, and smallpox. But with regard to diphtheria this announcement cannot be made with equal stress, as *recurrent attacks* are by no means rare. We have frequently seen patients suffer from a second attack before leaving the hospital. Also children have been

admitted to the hospital a second time, and, in two or three instances, a third time suffering from diphtheria, after intervals of a few weeks to three or four years.

Age.—The diphtherial infection finds in children the most favorable soil for its reception and propagation. The disease is exceedingly common among children up to the age of ten years, but those from one to five years are most susceptible. Some writers state that diphtheria attacks but seldom infants under a year old, and that in the first half-year of life there is complete immunity to the disease. It has fallen to our lot to see a large number of infants suffer and perish from this scourge, and many of them were under the age of six months. We believe, however, the infection is not so readily received at this early age. Adults not infrequently acquire the disease; but their chance of escaping it or of recovering when attacked is much greater than is the case with children.

It is a recognized fact that in all epidemics of diphtheria as well as in endemics children are the first to suffer from the disease. They also furnish the principal part of the mortality. This will be considered more fully under the head of prognosis. It is worthy of notice that the laryngeal form of diphtheria is limited almost entirely to children.

The following table shows the diphtheria patients admitted to the Municipal Hospital of Philadelphia during the last decade classified into age groups:

Year.	Under 1 year.	1-5 yrs.	5-10 yrs.	10-15 yrs.	15-25 yrs.	25 years and upward.	Total.
1893 . .	8	82	53	18	36	25	217
1894 . .	16	218	120	31	52	28	465
1895 . .	25	327	187	46	56	65	706
1896 . .	33	404	276	71	49	36	869
1897 . .	34	560	437	126	89	49	1295
1898 . .	42	552	447	93	47	48	1229
1899 . .	38	659	462	102	62	50	1373
1900 . .	40	595	473	117	90	52	1367
1901 . .	30	374	287	106	56	36	889
1902 . .	38	305	159	40	33	26	601
Total	299	4076	2901	750	570	418	9011

This table bears out the statement that children from one to five years of age are most susceptible to diphtheria; and also shows that the susceptibility diminishes very considerably after the age of ten years. We would direct attention to the table as showing the large number of infants that have come under our care. As parents are naturally loath to send children of this tender age to a hospital it is not improbable that the table shows a smaller proportion of patients under the age of one year than if the entire number in the city were considered.

Sex.—It scarcely seems probable that sex should exert any influence over susceptibility to diphtheria. It has been stated, however, by some observers that up to the age of four years there is no difference in susceptibility, but subsequent to this age males suffer more frequently than females.

The last census report of the United States shows that for the census year the deaths were quite equally distributed between the two sexes—14,878 were males and 14,081 were females. This very extensive statistical evidence warrants the conclusion that predisposition to the disease is not influenced by sex, and that where any disparity is found it is accidental rather than otherwise.

The following table shows the number of patients admitted to the Municipal Hospital each year during the last decade divided as to sex

Year	Males.	Females.	Total
1893	94	123	217
1894	214	251	465
1895	316	391	706
1896	484	445	929
1897	636	659	1295
1898	562	667	1229
1899	641	732	1373
1900	669	699	1367
1901	416	472	889
1902	285	316	601
Total	4256	4764	9011

It is worthy of remark that of the diphtheria admissions to the Municipal Hospital, Philadelphia, the females have exceeded the males. The table shows that this was the case every year during the last decade.

Race.—It cannot be said that race plays any prominent part among the predisponent causes of diphtheria. The opinion expressed by some observers that the Jews are especially liable to the disease cannot be accepted in the absence of positive proof. It is true in some of the large cities of this country the Russian Jews furnish a large contingent of the cases admitted to hospitals for infectious diseases, but this may be explained by the unsanitary environments of these people. The colored race has been thought to possess a considerable degree of immunity, but we have found no material difference between the death rates of the white and colored patients.

THE BACTERIOLOGY OF DIPHTHERIA.

In 1883 Klebs first observed and reported the constant presence of a bacillus in the false membranes in diphtheria patients.

The following year Loeffler¹ isolated these organisms in pure culture and demonstrated their pathogenic power by reproducing the disease by inoculation of the mucous membranes of animals.

Roux and Yersin² studied the effects of the diphtheria toxin elaborated by the bacilli, an investigation which led up to the development of serotherapy.

By 1891 the requisite postulates of Koch concerning the specificity of the germ had been fulfilled as regards the diphtheria bacillus. Its

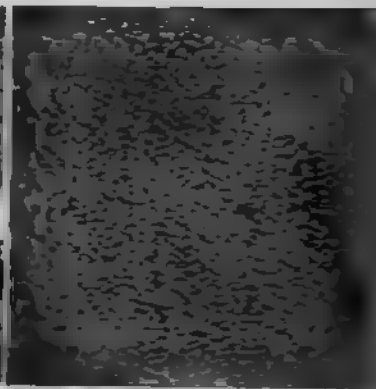
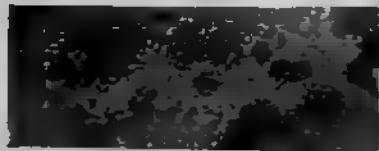
¹ Mittheil. aus dem Kaiser Gesundheitsamte, 1884, Bd. xi.

² Ann. de l'Institut Pasteur, 1888-1889.

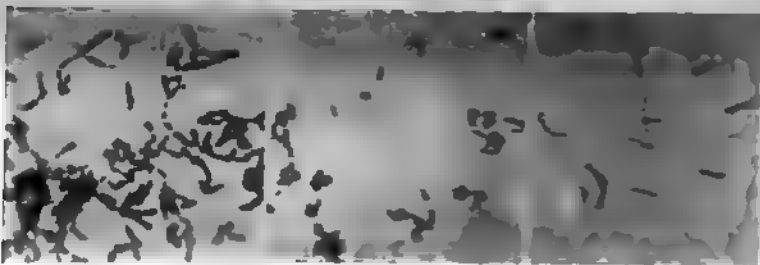
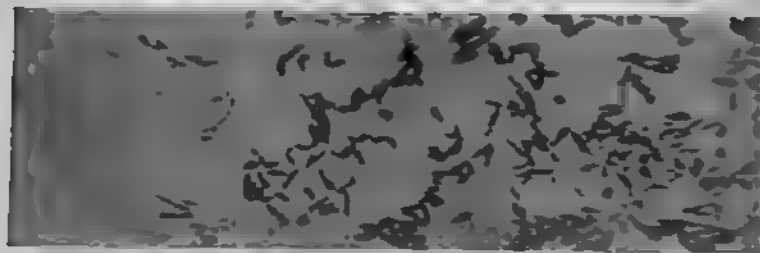
PLATE LVII.



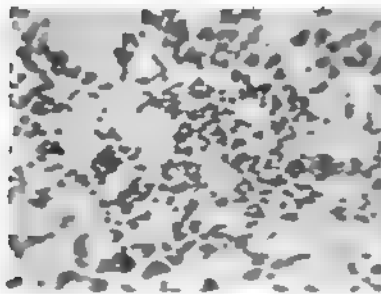
a. *Cryptosporidium parvum* (x1000)



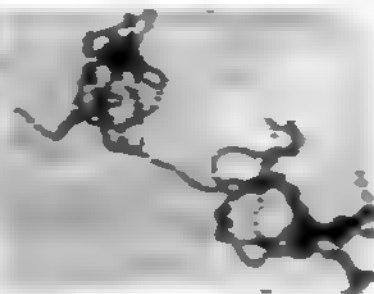
b. *Cryptosporidium parvum* (x1000)



c. *Diphtheria* (x1000) *Pseudomonas* (x1000) *Staphylococcus* (x1000)



Diphtheria (x1000)



Pseudomonas (x1000)

Diphtheria (x1000) *Pseudomonas* (x1000) *Staphylococcus* (x1000)

constant presence, its isolation in pure culture, the reproduction of the disease in animals by inoculations of pure cultures, the presence of the bacilli in the original and in the experimentally induced disease, demonstrated the bacillus of Klebs and Loeffler to be the cause of diphtheria.

Morphology.—The diphtheria bacillus is a straight or slightly curved, rod-shaped organism with rounded ends; the diameter is ordinarily from 0.5 to 0.8 microns and the length from 2 to 3 or more microns.

It is subject to the greatest variation of form; this is true to such an extent that polymorphism is an important characteristic.

Abbott¹ says that spindle and club shapes are extremely common, and that not rarely many of the rods stain irregularly; in some of them very deeply stained round or oval points can be detected. He adds: "When cultures are examined microscopically it is especially characteristic to find irregular, bizarre forms, such as rods with one or both ends swollen, and very frequently rods broken at irregular intervals into short, sharply defined segments, either round, oval, or with straight sides." The form and size of the bacillus vary greatly according to the culture medium used; it is smallest and most regular on glycerin agar; on Loeffler's blood serum one sees, "instead of the very short spindle, lancet, club-shaped, always segmented and regular staining forms as seen upon glycerin agar, long sometimes, extremely slender, sometimes thicker, irregular-staining threads that are usually clubbed and frequently pointed at their extremities."

In 1900 Wesbrook read before the Association of American Physicians a carefully prepared article on the various morphological types of diphtheria bacilli. He divided them into three groups—the granular (those with deeply staining granules), the barred (those with transverse bands), and the solid or evenly staining forms. Further subdivisions of these groups were discussed.

The granular type of bacillus is the one most commonly seen in the beginning of the disease; later these give way wholly or in part to the barred or solid forms; solid types may sometimes be replaced by the granular when convalescence is established and just before the throat begins to clear. Wesbrook's findings have been more recently confirmed by Gorham.

The relation of the solid forms to true diphtheria bacilli is still unsettled. They are said to be sometimes encountered as variants in pure cultures of diphtheria organisms. Certain of the solid forms have characteristic: which seem to distinguish them from the diphtheria bacillus and to class them with the pseudodiphtheria organisms. For instance, some of the solid forms fail to produce acid in dextrose bouillon, a property which is possessed by the true diphtheria bacilli.²

Staining Properties.—The diphtheria bacillus stains well with the ordinary aniline dyes and with the Gram stain. The best results are,

¹ Principles of Bacteriology, fifth edition.

² Statements made in a report on "Diphtheria Bacilli in Well Persons" by a Committee of the Massachusetts Association of Boards of Health, Boston, 1902.

however, obtained with Loeffler's alkaline solution of methylene blue, which brings out the granules well. This solution is made up of

Concentrated alcoholic solution of methylene blue	20 c.c.
Caustic potash in 1 : 10,000 solution	100 "

Neisser Stain.—The stain suggested by Neisser in 1897 is said by Abbott to enable one to overcome in a very large part the difficulty occasionally experienced in differentiating the diphtheria bacillus from other throat organisms which may simulate it. The method is described by Abbott as follows: The culture to be tested should be grown upon Loeffler's blood-serum mixture solidified at 100° C.: it should develop at a temperature not lower than 34° C. and not higher than 36° C., and it should be not younger than nine and not older than twenty-four hours. A cover-glass preparation made from such culture is stained for from one to three seconds in the following solution:

Methylene blue (Grubler's)	1 gram.
Alcohol (96 per cent.)	20 c.c.

When dissolved, mix with

Acetic acid	50 c.c.
Distilled water	200 "

After thoroughly rinsing in water the preparation is then stained for from three to five seconds in vesuvin (Bismarck brown), 2 grams dissolved in a litre of boiling distilled water, filtered and allowed to cool. It is again rinsed in water and examined as a water-mount or dried and mounted in balsam.

When so treated the bacilli appear as faintly stained brown rods in which from one to three brown granules are always to be observed. The dark granules are at one or both poles of the cell, are more or less oval, and usually seem to bulge a little beyond the contour of the bacillus in which they are located. In the vast majority of cases it seems safe to regard all bacilli that do not stain in this manner as distinct from bacillus diphtheriae (Abbott).

Biological Characters.—The diphtheria bacillus is aerobic, non-motile and liquefying, and does not form spores. It grows freely in the presence of oxygen, but is also a facultative anaerobic (Sternberg).

The diphtheria bacillus is destroyed by exposure to a temperature of 58° C. (136° F.) for ten minutes. In the dried state it may maintain its vitality for a long period. Park found active bacilli on dried membrane after seventeen weeks, and Roux and Yersin living but non-virulent bacilli after five months. Bacilli were found by Abel to persist for five months on children's toys kept in the dark. When the organisms are preserved in sealed tubes and protected from light and heat they may remain virulent for years.

Growth on Loeffler's Blood Serum.—This is the best medium for the growth of the diphtheria organism and the one which is ordinarily employed for the culture test. It is a mixture of three parts of blood serum with one part of bouillon, containing 1 per cent. of peptone,

1 per cent. of grape-sugar, and 0.5 per cent. of sodium chloride; the mixture is sterilized and solidified at a low temperature (Sternberg).

The diphtheria organism grows so much more promptly upon this mixture than other mouth and throat bacteria that at the end of twenty-four hours the diphtheria colonies may be readily recognized while the other colonies are still inconspicuous.

Growth on Glycerin Agar.—The development upon this medium is much more delicate and less luxuriant than upon blood serum. The colonies appear at first on the surface as flat, almost transparent, dry, non-glistening, non-elevated round points. When slightly magnified they are seen to be granular with an irregular central marking. The colonies are always dry in appearance; the deep colonies are coarsely granular (Abbott). Bacilli taken directly from the throat develop poorly, or not at all, on agar, but subcultures may grow very well.

Growth on Gelatin.—The colonies on gelatin do not present their characteristic appearance in less than three days. If slightly magnified the colonies show a denser centre than periphery; the border is notched. The colonies are granular, particularly the deep ones (Abbott).

Growth on Bouillon.—According to Abbott, the growth on bouillon produces fine clumps which fall to the bottom of the tube or become deposited on its sides without causing diffuse clouding. Sometimes the clumps cannot be discerned by the naked eye. The reaction of the bouillon is at first acid and later alkaline. According to Schabad the maximum acidity occurs most often on the second day, although sometimes it may be on the third and rarely on the fourth or later.

Many observers regard the acid formation a feature of importance in distinguishing between the diphtheria and pseudodiphtheria organism; the value of this test, however, is not yet definitely determined.

Growth in Milk.—Sternberg states that milk is a favorable medium for the growth of the diphtheria bacillus and adds that, as it grows at a comparatively low temperature (20° C.), this fluid may become a medium for conveying the bacillus from an infected source to throats of previously healthy children. The appearance of the milk remains unchanged.

Growth on Potato.—Welch and Abbott state that the diphtheria bacillus grows on ordinary steamed potato without any preliminary treatment, but that the growth is usually entirely invisible or is indicated by a dry, thin, glaze after several days. At the end of twenty-four hours, at a temperature of 35° C., microscopic scrapings of the potato reveal a decided increase of the bacilli.

Pathogenesis.—According to Park the diphtheria bacillus is pathogenic for guinea-pigs, rabbits, chickens, pigeons, small birds, and cats; to a less extent it is pathogenic for horses, cattle, dogs, and goats, but not for rats and mice. The rat and the mouse exhibit a remarkable insusceptibility; a dose of 2 c.c. of a bouillon culture will kill a rabbit, but not a mouse.

The inoculation of such animals as cats and rabbits by rubbing a pure culture of the diphtheria bacillus upon the mucous surface of the

opened trachea produces a disease which is essentially the same as that seen in man. The animal usually dies in from two to four days, not from a general invasion by the diphtheria organism, but as a result of the absorption of the soluble toxins formed at the seat of infection.

The wound at autopsy is covered with a grayish, adherent, necrotic, distinctly diphtheritic layer. The surrounding subcutaneous tissues are cedematous and the lymphatic glands at the angles of the jaw are swollen and reddened. The mucous membrane of the trachea at the site of inoculation is covered with a firm, grayish-white, loosely attached pseudomembrane identical in all respects with that seen in human diphtheria. The membrane and the cedematous fluid about the wound show the presence both by smears and by culture of the diphtheria bacillus (Abbott).

In animals that did not die too quickly Roux and Yersin have noted the development of paralysis of the posterior extremities.

It is a well-established fact that the diphtheria bacillus under ordinary circumstances remains in the vicinity of the site of inoculation. When it is found in the blood or visceral organs its presence is probably accidental. The widespread changes in important organs in diphtheria must therefore be ascribed to a diffusible circulating poison produced by the diphtheria organism in its original nidus. That such is the case was proved by Roux and Yersin in 1888, when they demonstrated the presence of a poison in diphtheria cultures which were filtered through porous porcelain. It was found that old cultures and particularly those of alkaline reaction, had a much greater toxic potency than recent cultures of acid reaction. Injection of filtered cultures into susceptible animals produced local edema, congestion and hemorrhage of the internal organs, effusion into the pleural cavity, etc. It is thus seen that practically all of the symptoms produced by the injection of pure cultures of bacilli may be obtained by injection of the filtered cultures save the production of a false membrane. Sternberg remarks that this deadly toxin appears to be an albuminoid substance (a toxalbumin), but its exact chemical composition has not yet been determined.

Virulence and Avirulence of Diphtheria Bacilli.—When virulent bacilli are grown in bouillon, soluble toxins are developed which produce certain noxious effects upon guinea-pigs. Even where the bacilli are removed by filtration the injection produces death of the animal. Practically all bacilli derived from clinical cases of diphtheria produce toxins with these properties. Conversely, it would seem that bacilli that produce no toxins in bouillon will not produce them in the human subject. Westbrook and Gorham rather dissent from the view generally accepted, and believe that animal inoculation of cultures is no definite test of virulence of the bacilli in the human species.

Formerly the non-virulent bacilli were classed by some writers in a group apart from the genuine diphtheria organism. It is now pretty generally recognized that true diphtheria bacilli may possess varying grades of virulence. Those occurring in the throats of convalescent patients and those found in the throats of healthy persons have fre-

quently a very low grade of virulence. The less virulent forms commonly increase in numbers as progress toward the recovery of diphtheria advances.

The Distribution of Diphtheria Bacilli in the Body.—Abbott says: "In a certain number of cases diphtheria bacilli have been found in the blood and internal organs of individuals dead of the disease; but all that has been learned from study of the secondary manifestations of diphtheria tends to the opinion that they are in no way dependent upon the immediate presence of bacteria and that the occasional appearance of diphtheria bacilli in the internal organs is in all probability accidental, and usually unimportant."

General infection with the diphtheria bacillus has been reported by a considerable number of writers.

Frosch¹ was the first to note the presence of diphtheria bacilli in the internal organs of patients dead of diphtheria; he found them in the heart's blood, liver, spleen, kidney, and lymph nodes in 10 out of 15 cases examined.

Kutscher found the bacilli in 8 out of 9 cases in the lung. Kanthack and Stevens found them in the spleen in 10 out of 21 cases, in the kidney in 2 out of 3 cases, and in the lungs in each of 26 cases.

Wright and Stokes, in a report of 31 cases, found the diphtheria organism 30 times in the lungs, 9 times in the liver, 7 times in the mesenteric lymph nodes, 5 times each in the spleen and heart's blood, 4 times in the cervical lymph nodes, and twice each in the brain and bronchial glands.

Genersisch examined 25 cases of septic diphtheria in some of which he failed to find the streptococcus in the blood or internal organs; he concluded that the diphtheria bacillus was capable alone of producing septic symptoms. Stephens and Parfitt have reported a case of general infection with the diphtheria bacillus in which these organisms were recovered from the blood during life. In a child with an unusually high and unexplained temperature, suffering from diphtheria at the Municipal Hospital, we recovered the diphtheria bacillus in pure culture from the blood a day before death.

Councilman, Mallory, and Pearce have extensively cultured the various organs in 161 diphtheria autopsies. They found bacilli in the heart's blood in pure culture 7 times, and 4 other times in association with other organisms. Diphtheria bacilli were found in the liver 30 times, in the spleen 19 times, and in the kidneys 27 times. These investigators remark, apropos of these findings: "Whether the diphtheria bacillus does or does not continue to produce the toxic products wherever it may be in the blood or internal organs it is impossible to say, but from the number of fatal cases with such an infection it would seem very probable that it does. Kanthack and Stephens, and Genersisch also, incline to this opinion.

Diphtheria bacilli have been thrice found upon the vegetations of an acute ulcerative endocarditis. These have been reported by Howard,

¹ *Zeitschr. f. Hygiene und Infektionskr.*, 1893, Bd. xlii. pp. 49-52.

Wright, and Councilman, Mallory, and Pearce. The antrum and accessory nasal sinuses may harbor diphtheria bacilli for a long time. Wolff, in autopsies on 15 severe cases of diphtheria, found diphtheria bacilli in the antra in 12. Councilman, Mallory, and Pearce examined the antra in 52 cases; in 16 of these diphtheria bacilli were recovered from both sides. They suggest that infection of the antra may explain the persistence of the bacilli in the nasal discharge for protracted periods.

The middle ears were examined in 144 cases. In 86 they were found diseased, and in 37 diphtheria bacilli were recovered from one or both ears. They were usually found in association with other bacteria.

Persistence of Diphtheria Bacilli in the Throat.—Virulent bacilli may persist for varying periods in the throats of persons who have recovered from diphtheria. In the vast majority of cases they disappear in from one to two weeks after the disappearance of the membranous exudate. Park and Beebe, in a study of 605 consecutive cases, found the bacilli absent within three days after the disappearance of the membrane in 304; in 176 cases they persisted for seven days; in 12, for three weeks; in 4, for four weeks, and in 2, for nine weeks. Later, Park saw a case in which the bacilli were found for six months. Abbott has observed a case in which the cultures examined remained positive for 128 days. In the Boston City Hospital, where three negative cultures are required before the patient is discharged, cases have been detained for six, seven, eight, and nine weeks, and even three months, on account of the persistence of bacilli in the nose. Le Gendre and Pochon described in 1895 a case in which the bacilli persisted in the nose for fifteen months after an attack of nasal diphtheria.

Diphtheria Bacilli in the Throats of Healthy Persons.—There are two factors necessary for the production of diphtheria—the presence of the specific bacillus and the existence in the host of susceptibility to the disease. Many persons appear to be able to harbor virulent diphtheria bacilli in their throats without contracting the disease. In 1894 Park and Beebe examined the throats of 330 healthy persons who had not, as far as was known, come in contact with persons suffering from diphtheria. Of this number virulent bacilli were found in 8, 2 of whom later developed the disease. In 24 of the 330 healthy throats non-virulent or attenuated forms of the diphtheria organisms were found.

This question has been recently studied with care by a Committee of the Massachusetts Association of Boards of Health, composed of men of high scientific standing.¹ We quote freely from the report:

"All observers are not in accord as to the morphological appearances which are to be considered as characteristic of the diphtheria organism. That there is considerable divergence of opinion among bacteriologists as to what should be classed as genuine diphtheria bacilli is evidenced by the great discrepancy in the prevalence of diphtheria organisms in the throats of well persons as reported by different investigators. In Boston about 1 per cent. were considered positive; in Brookline (Mass.),

¹ Report on Diphtheria Bacilli in Well Persons, Journal of the Massachusetts Association of Boards of Health, July, 1902.

2.3 per cent.; in Lowell, 1.2 per cent.; in Springfield, 1.6 per cent.; in Providence, 9 per cent., and in the District of Columbia, 22 per cent."

The committee states that it feels justified in the inference that in urban communities at least 1 to 2 per cent. of all well persons among the general public are infected with genuine diphtheria bacilli, and exposed persons in families and schools in from 8 to 50 per cent. of the cases.

There are two classes of persons carrying diphtheria bacilli in their throats—those exposed to the disease and those in whom no exposure is known. Among the general unexposed public about 3 per cent. of the people have typical diphtheria bacilli in their throats. In the eastern part of the United States it is 1.39 per cent.

"This would mean in Boston, if the smaller figure be used, about 8000 such cases." The committee concludes that "it is impracticable to isolate well persons infected with diphtheria bacilli if such persons have not, so far as known, been recently exposed to the disease." The committee likewise believes that "it is not advisable as a matter of routine to isolate from the public all the well persons in infected families, schools, and institutions." It does, however, counsel that children in infected families should be kept away from school and public places, and that milkmen should not be allowed to continue their business.

In considering the virulence of the bacilli found in healthy throats, it is shown that only about 17 per cent. of the 1 to 2 per cent. of persons harboring diphtheria bacilli have virulent bacilli which are dangerous to the public health.

Diphtheria Bacilli in Persons Exposed to the Disease.—Park found 50 per cent. of the children exposed to diphtheria in New York tenement houses to have Klebs-Loeffler bacilli in their throats. Chapin, in Providence, found bacilli in 16 per cent., and Kober, in Breslau, in 8 per cent. The bacilli in the throats of healthy exposed persons are probably of the same virulence as those in the diseased individual, and such persons should therefore be isolated, according to the committee above mentioned, until free of the bacilli.

Pseudodiphtheria Bacilli.—Considerable diversity of opinion exists among bacteriologists at the present time as to the proper classification of certain bacilli which are morphologically and tinctorially identical with the diphtheria organism, but which differ from it in other respects.

There appear to be two schools of opinion upon the subject, the one proclaiming the identity of the diphtheria and diphtheria-like bacteria and the other asserting that they belong to separate and distinct classes.

Most writers agree that the non-virulent and non-toxic Loeffler bacilli are to be regarded as true diphtheria organisms which have merely suffered attenuation.

There are, however, other organisms which resemble the diphtheria bacillus very closely, but differ therefrom not only in the absence of toxin production, but also in certain other particulars. Among these may be included the so-called xerosis bacillus, which is commonly found in the eyes in the condition known as xerosis conjunctivæ.

According to Park, "the variety of pseudodiphtheria bacillus most commonly seen is rather short, plump, and more regular in size and shape than the Klebs-Loeffler bacillus. On blood serum the growth is much like that of the true diphtheria organism. The great majority of bacilli in any culture show no polar granules by the Neisser method and stain solidly with Loeffler's methylene-blue solution. They do not produce acid in glucose bouillon. They are found in about 1 per cent. of normal throats and noses. Neisser's stain is of value in these cases, but, unfortunately, the absence of the stained bodies is not sufficient ground to exclude the possibility of their being true diphtheria bacilli."

Schabad¹ has made a careful study of the various methods of differentiating between genuine diphtheria and pseudodiphtheria bacilli. He concludes as follows:

1. Diphtheria bacilli and pseudodiphtheria bacilli are two distinct organisms.
2. The difference between them lies in their growth in different culture media (especially agar and ascitic fluid), in their morphology, reaction in bouillon culture, coloration with Neisser's stain, and pathogenesis for animals.
3. Neisser's stain and the reaction in bouillon are the most important means of differential diagnosis.
4. Avirulent diphtheria bacilli should be distinguished from pseudodiphtheria bacilli; they are in all respects identical with virulent diphtheria bacilli save in their lack of virulence.
5. To the mistaking of avirulent diphtheria bacilli for pseudodiphtheria bacilli is attributable the failure of many writers to attain definite results with Neisser's stain and reaction in bouillon.
6. Avirulent diphtheria bacilli can, in all cases, be distinguished by the above methods from pseudodiphtheria bacilli.

A diphtheria-like bacillus which produces little or no acid in a bouillon culture, which does not show typical polar granules when stained by the Neisser method, and which will not kill guinea-pigs, may be set down as a pseudodiphtheria organism. Such a bacillus will not produce diphtheria in the human subject, and its presence in healthy throats need not give concern.

INCUBATION PERIOD.

Incubation.—The period of incubation is the interval between the moment of receiving the infection and the beginning of symptoms. It is believed that this period may vary somewhat according to the activity or virulence of the infecting organism and the receptivity of the individual. When the organisms lodge upon a mucous membrane which is readily penetrated the diphtherial process is apt to appear sooner than where this membrane has greater resistance.

Where the conditions are favorable the bacilli doubtless begin their

¹ Beitrage zur diff. diag. des Diph. u. Pseudodiph. bacillus, Jahrbuch f. Kinderheilk., October, 1901, quoted by Northrup, article on Diphtheria, Nothnagel's Encyclopedia of Practical Medicine.

work as soon as they have effected a lodgement, but changes at the seat of disease are not recognized until the process is sufficiently far advanced to show the characteristic exudate. The constitutional disturbances, such as fever and other subjective symptoms, usually do not appear until the local manifestations have reached a certain degree of intensity. It is quite possible, therefore, that mild cases may not be recognized as early as severe ones, and thus the period of incubation among the former may sometimes appear to be longer.

Some observers believe that this period is shorter during the epidemic prevalence of diphtheria, especially when of a malignant type, than when the disease occurs sporadically. In most cases it is difficult to determine the exact moment of infection. This can only be known when there has been but a single exposure. It would seem that there should be no difficulty in determining the period of incubation from observations in a large hospital, and yet we find that nurses and other attendants who take diphtheria fall ill at variable periods after commencing work. In the vast majority of instances, however, the symptoms of the disease appear during the first week of service. Occasionally a nurse will work for three or four weeks before manifesting any evidence of infection. One of our nurses performed her duties for one year before she fell ill with diphtheria. It is evident, therefore, that the infecting organisms may find in an individual a more favorable soil at one time than at another, and this variation of susceptibility adds to the difficulty of establishing the period of incubation.

There is no doubt, however, that in comparison with most other infectious diseases the period of incubation of diphtheria is relatively short. Most observers fix the period from two to three days; some believe that it may vary from one to eight days, and others allow that in exceptional cases it is as long as twelve to fourteen days. We believe that in the vast majority of instances it is from two to five days.

Lennox Browne says: "The experimental incubation period, when communicated by inoculation in the lower animals, is short, and varies from twelve hours to three days. It is said to be about the same period when a human patient is infected by direct contact, and our own experience leads us to concur that the disease is not infrequently developed at the minimum interval.

"Leslie Phillips reports a very interesting case in which some of the same instruments were used on the same day, first in the operation for tracheotomy for diphtheria, and, secondly, for circumcision; the circumcised child had pseudomembrane on the prepuce on the fourth day.

"In ordinary circumstances, the period between the exposure to the contagion and the appearance of false membrane in the throat is probably from one to four days. A longer interval is exceptional."

THE SYMPTOMATOLOGY OF DIPHTHERIA.

Not infrequently the characteristic symptoms of diphtheria are preceded by slight indisposition, such as lassitude, loss of appetite, headache, nausea and sometimes vomiting, and general malaise. These prodromes, however, are not distinctly different from what may be seen in many other affections. There may be slight stiffness of the neck, with hyper-sensitive lymph glands near the angle of the jaw, and a little inconvenience experienced in deglutition. On inspection the fauces may be found hyperæmic. There may be mild chilly sensations, and, in children, convulsions sometimes occur. The temperature is apt to be only slightly elevated. These mild symptoms rarely continue longer than a few hours before the true nature of the disease is revealed.

Vomiting is by no means so constant a precursory symptom of diphtheria as of scarlet fever. The pain in the fauces and at the angle of the jaw is but slight as compared with that experienced in ordinary tonsillitis. Indeed, the comparative absence from pain at this stage of the disease is of considerable significance in the matter of diagnosis. There may be diarrhoea or constipation; one is just as liable to be met with as the other. The fauces often feel dry, and there is a disposition to hawk and clear the throat.

When the disease is going to assume the laryngeal form, the voice, often at an early stage, becomes husky, even before any membrane has appeared. Along with this symptom there is very commonly a shrill, brassy cough, and sometimes slight dyspnoea, resulting from a mild spasmodic affection of the larynx.

Throat.—The first positive evidence of diphtheria is usually seen in the throat. As stated under the head of etiology, the tonsils seem to favor the lodgement and propagation of the specific bacilli; for in the vast majority of cases it is on these glands that the disease process begins. The fauces are commonly red and inflamed, and the tonsils may or may not be swollen, although in most cases the swelling is marked. Small spots of exudate now appear on their surface or in their crypts—the latter being a common seat of this process. In mild cases this condition does not increase. It is then difficult to distinguish between diphtheria and tonsillitis without the aid of bacteriological examination. Patients with the latter affection are often sent to the hospital on a mistaken diagnosis.

In the better-marked form of the disease the small patches of exudate rapidly spread, covering not infrequently the entire tonsillar surface in less than twenty-four hours. This local manifestation may be confined to one tonsil, but more often involves both. When the exudate is limited to the tonsils the liability to secondary systemic infection is not very great.

In the severe forms of diphtheria the exudate spreads beyond the region of the tonsils, or it may appear simultaneously on various parts of the fauces. One of its peculiarities is that it often shows itself as small, thick patches on prominent points, such as the end of the uvula,

the edge of the epiglottis, the cartilage of Wrisberg, and the like. It very frequently covers completely not only the tonsils, but the anterior and posterior pillars, the pharyngeal wall, the uvula, and the entire soft palate. In severe cases it is not uncommon to see the exudate on the vault of the mouth piled up so high as to form a thick spongy mass, seriously interfering with deglutition. At the time of writing these lines we have in the hospital three or four patients in whose throats this extensive form of exudate is seen. The clinical history of one of these patients is as follows:

E. R., aged seven years, white, female, admitted December 7th, on ninth day of the disease. On the first and second days in the hospital the temperature was 100° F., on the third day it fell to 97 $\frac{4}{5}$ ° F. The pulse ranged from 104 to 112 per minute during the first and second days, and on the third day fell to 82. The culture was positive. On admission the exudate covered completely and thickly both tonsils, the anterior pillars, the pharyngeal wall, the uvula, and the greater part of the soft palate. On the latter it was piled up in a thick, spongy mass. Deglutition was difficult. The face was swollen, pale, and glossy. The breath was very fetid. Both nares contained large plugs of exudate, and were constantly oozing blood. The cervical glands on both sides of the neck were very much swollen. Immediately after admission the patient received 4500 units of antitoxin; twelve hours later another dose of 3000 units was given, and again a third dose of 4500 units, making in all 12,000 units. Death resulted on December 9th, from toxæmia and exhaustion.

We have seen the exudate even more copious than in the case just cited. Cases have come under our observation in which not only the entire fauces, including the soft palate, were covered, but even the hard palate and the greater part of the buccal cavity also. Sometimes it appears on the gums, but more often invades the edges of the tongue. It is frequently seen in the pharyngeal vault, and may extend into the Eustachian tubes. The nares and the larynx are so often involved that the behavior of the disease in these cavities will subsequently receive special notice.

The exudate is usually of a yellowish-white or cream color, but it may present a dark-gray appearance. Its color is liable to be changed by the ingestion of certain drugs, or by remedial agents employed locally. It sometimes is rendered darker by having coagulated blood incorporated with it. But in perfectly typical cases it does not look unlike moist chamois skin. Indeed, when large fragments or casts are exfoliated and floated in water they have a strong resemblance to this material.

The exudate may be thick, or thin and filmy. When very thick it may be seen, even at quite an early state, lying rather loosely on the mucous membrane, or partly detached at its margin, especially when located on the soft palate. If forcibly removed it is liable to be reproduced in the course of a few hours, although in many cases it exfoliates quickly and does not reform. Instead of presenting the appearance of

a distinct membrane lying upon the mucous surface, the exudate sometimes forms into and becomes a part of the mucous membrane itself. In this case there is a grayish discoloration which disappears slowly, and often by the process of necrosis, rather than by exfoliation of the membrane. Of course, this process is followed by an ulcerating surface which heals by granulation.

The involved parts of the fauces, especially the uvula, become oedematous and swell considerably. After the exudate has disappeared from the uvula, the latter is apt to present an ulcerated appearance, and, through loss of tissue, is not infrequently left smaller than normal. In all severe cases in which there is oedema and swelling of the fauces there is not only difficult and painful deglutition, but the respiration and articulation are also affected.

In the act of swallowing it is not uncommon to see milk regurgitated through the nares. As the case progresses the voice becomes distinctly nasal, and is apt to continue so for some weeks.

At first the exudate is free from odor; but when the disease is severe a distinct odor is noticed in the course of two or three days. Indeed, the breath of the patient is often so peculiarly offensive that an experienced clinician might be led to suspect the nature of the affection before an examination of the throat has been made. In septic cases, when decomposition of the secretions and the exudate goes on rapidly, the odor is in the highest degree offensive, and is well calculated to excite suspicion that extensive necrotic changes of the tissues may be taking place. The tissue change, however, is not always as great as the odor would indicate. A copious mass of exudate is often thrown off very quickly by the process of exfoliation, leaving the parts only slightly ulcerated. In such cases the odor will promptly disappear, especially with the use of cleansing or antiseptic lotions. With this apparent improvement one should not be too hasty in pronouncing the patient out of danger, for the probabilities are that the most critical period of the disease is yet to be encountered. Where the mucous lining of the fauces is at all destroyed, leaving the absorbents exposed, the toxin of the specific micro-organisms is permitted to enter the circulation, and the subsequent danger from toxæmia is far greater than the primary local disease.

While there is usually some swelling and tenderness of the cervical and submaxillary glands at an earlier stage of the diphtherial process, coincidently with intense involvement of the fauces, these glands, together with the surrounding areolar tissue, become indurated and infiltrated, giving rise often to extensive tumefaction. The face, besides being pale and sallow, presents also a swollen and glossy appearance. As the exudate and septic secretions disappear from the throat, the tumefaction of the neck subsides. Occasionally, however, the cervical glands take on suppurative action, but not so frequently as in scarlet fever.

Nose.—Next to the fauces the nose is the most common site of the diphtheritic process. The disease not infrequently attacks the nares

primarily, but most often the exudate extends from the throat to the nasal cavities by way of the posterior aspect of the uvula. When this occurs the posterior wall of the pharynx is also liable to be involved through contiguity of structure. At first there is but little discharge from the nares, as in the beginning of an acute catarrh, but it soon increases and becomes flocculent. When the disease has fully developed, the discharge is often profuse and sometimes fetid.

Before the diphtherial process has continued very long, evidence of copious exudation may be seen by inspecting the nares. In many cases the membrane is very thick and dense, and occludes the nasal cavities completely. There is then but little discharge from the external orifices; but the voice becomes distinctly nasal, and the patient is obliged to breathe through the mouth.

When the fauces are at the same time severely involved, the respiration becomes considerably hampered, and there is also difficult deglutition, with marked restlessness and insomnia.

The amount of exudate that is sometimes expelled from the nares is enormous. The membrane is often thrown off in perfect casts, and on inspecting these one is apt to feel surprised that so much material could have been contained within the nasal cavities. When the exudate begins to separate, or has been either partly or wholly cast off, the discharge usually returns, and is often sanguinopurulent in character. There is no form of diphtheria more dangerous than that of the nares. The injury sustained by the capillary bloodvessels prepares the way for rapid absorption of the toxins, the effects of which are apt to become painfully visible in a short time. Not only is systemic poisoning seen, but the more common sequelæ of diphtheria most often follow the nasal form of the disease.

Epistaxis is of frequent occurrence even in mild cases; but when the diphtheritic involvement is intense the hemorrhage from the nose is liable to occur repeatedly, as the disease progresses, and may prove to be a very troublesome symptom. In some cases there is a constant oozing of blood, while in others the hemorrhage is sometimes so free as to be the immediate cause of death.

In the severest form of nasal diphtheria the nose is slightly reddened externally, and moderately swollen or œdematous. The face also is œdematous, remarkably pale, and has a peculiar glistening appearance. The pulse is usually feeble, the circulation bad, vomiting often occurs, and not infrequently there is marked drowsiness. Indeed, the symptoms, taken together, are such as would indicate profound systemic poisoning. Many patients in this condition die at a comparatively early stage of the disease.

In the more favorable cases the exudate is thrown off *en masse* in the form of casts, and the constitutional symptoms do not become so pronounced. But one should not feel too sanguine of recovery in any case, for danger of the development of toxæmia is never absent. Even when this serious condition does not arise, and the general symptoms seem most favorable, still there is a strong liability that the affection

may be followed by paralysis, either partial or general. Postdiphtheritic paralysis is more common after the nasal form of the disease than after any other variety.

Nasal diphtheria sometimes assumes the form of chronic rhinitis. In such cases there is usually a discharge from the nares and often excoriation of the skin about the nose. But the affection may persist for months, with little or no nasal discharge. Persons thus afflicted often unwittingly spread diphtheria. It is important that such cases should be recognized and treated, and even isolation should be advised until a cure is effected and the specific organisms have disappeared. It is only by the aid of bacteriology that this form of diphtheria can be definitely determined.

Middle Ear.—From the pharyngeal vault the exudate sometimes spreads by way of the Eustachian tube to the middle ear, causing an acute median otitis. This is often unattended by pain; hence the condition may not be recognized until suppuration takes place and the tympanum has ruptured. The purulent discharge which flows from the meatus will show the presence of the bacilli of diphtheria associated with certain other organisms, such as streptococci and staphylococci. There is usually some rise of temperature, often assuming a septic character.

The otorrhœa frequently persists a long time, but is seldom followed by permanent deafness. Temporary deafness, however, may be seen as the result of a parietic condition of the muscles of the Eustachian tube and of the tympanum. Only in rare instances are the changes in the intratympanic cavity so great as to cause permanent deafness. This is not so likely to happen in diphtheria as in scarlet fever.

Eyes.—Diphtheritic involvement of the conjunctiva is not very frequently seen. It occurs sometimes, but the wonder is that it is not more common in children, since they so often convey the infectious discharges from the nares to their eyes by means of their hands. Physicians and nurses who work among diphtheria patients are frequently subjected to the risk of infection by having the secretions from the throats of such patients coughed into their eyes. While we have sometimes seen a mild conjunctivitis occur from this accident we have never known it to assume a diphtheritic character, though such a result is not impossible.

It has been suggested by some writers that the diphtheritic inflammation may extend to the conjunctiva by way of the tear duct, but this we believe is of rare occurrence. As an unhealthy mucous membrane is more prone to diphtherial infection, it is therefore probable that an acute or chronic inflammation of the eyes furnishes a predisposition to eye involvement when diphtheria occurs in a child thus afflicted.

When the conjunctiva becomes involved the membrane usually spreads rapidly from one eyelid to the other, and the bulbar conjunctiva is almost always greatly chemosed. The exudate is first seen as flocculi, but it rapidly forms into a thick membrane, so thick, indeed, as to press hard upon the cornea, causing it to become hazy and often undergo a destructive necrosis. When the cornea of the eye becomes weakened

or perforated by this process the iris prolapses. During the course of the disease the eyelids swell and stiffen, so that it is almost impossible to inspect the eye itself. From what has been said it is evident that loss of vision is imminent.

Fortunately the affection is not always so destructive. In the milder cases recovery may take place without impairment of vision. But when the disease is so severe as to cause the destruction of both eyes, the patient's life is placed in great jeopardy. All such cases that have come under our observation have died.

Skin.—The diphtheritic membrane may appear on abraded surfaces of the skin, but this is by no means so common, even in the worst forms

FIG. 92



Diphtheritic involvement of the mucous membrane of the eyelids, showing thick, copious exudate on the inner surfaces of the lids, oedema of the face, and swelling of the glands of the neck. Vision was destroyed and death ensued.

of diphtheria, as has been supposed. It is only in the wound of the skin from the operation of tracheotomy that this condition occurs with any degree of frequency. But even here the diphtheritic membrane appears less often than one would suppose. We have, however, known the membrane to appear on the prepuce of a child who developed diphtheria immediately after circumcision.

Some writers describe a rash that is sometimes seen as the result of diphtheria. It is said that it may appear at an early stage of the disease, and that it is erythematous in character. It is described as either localized and evanescent, being scarcely visible for more than a few hours, or as covering a large surface of the skin and remaining for some days. We must confess that we are not familiar with any

rash that can be said to be pathognomonic of diphtheria. When a circumscribed or diffuse rash of punctiform character is present, one should think of scarlatinal infection, for scarlet fever and diphtheria not infrequently coexist. The former disease cannot necessarily be excluded because the body temperature is low. Over and over again we have seen these diseases coexist when the temperature was but little above normal.

Edema.—Edema of the face and some other parts of the body is sometimes seen as the result of intense systemic poisoning, and quite independent of disease of the kidneys.

In the worst forms of diphtheria it is not uncommon to find petechiæ, purpuric discolorations, and ecchymoses. The latter may occur spontaneously, or result from the slightest bruise.

Antitoxin rashes, so common since this agent has come into use, are postponed for consideration under the head of the antitoxin treatment of diphtheria.

Toxæmia.—A peculiar train of symptoms often results from absorption of the toxin elaborated by the specific organisms of diphtheria. These symptoms are so peculiar that one who is at all familiar with them would seldom fail to associate them with diphtheria, even in the absence of any other clinical manifestations of this disease. They often follow the disappearance of the exudate in the nose and throat, making their appearance at a time when the physician may feel that his patient is on the straight road to recovery.

When symptoms of toxæmia occur, they usually make their appearance during the second week of the illness. They may, however, be seen a little earlier or a little later. Frequently about the time the exudate has disappeared the patient commences to vomit, and the stomach becomes so irritable that everything is ejected almost as soon as swallowed. Pallor at once is noticed, and this rapidly increases, giving the face a remarkably blanched appearance. The change of color to a pale, waxy hue is sometimes so sudden as to come in the nature of a surprise. Coincidentally with these symptoms the pulse becomes weak and often irregular. It may be either slow or rapid. The force of the apex beat of the heart is diminished, and the first sound indistinct. As the case progresses, the pulse becomes weaker and slower, often not more than 40 to 50 per minute. The extremities are cold. The mind is clear, but the patient shows an anxious expression. Albumin is most always found in the urine. The temperature is apt to be low, often, indeed, subnormal.

When toxæmia is not profound the symptoms may gradually improve and recovery follow. But the condition of the patient should always be regarded as extremely critical. Often the signs of improvement are more apparent than real. For example, a patient may be entirely conscious, converse intelligently, sit up in bed and take nourishment, and, despite this apparent improvement, fall over and die almost instantly of heart-failure. More frequently, however, death comes gradually, and is almost invariably preceded by precordial pain. The

heart sounds become less and less distinct, and the pulse grows more and more feeble until it is absolutely lost. It is not rare for a patient to live for hours, sometimes even a day or two, with no perceptible pulse at the wrist. It is remarkable to note that consciousness in this condition is usually retained to the last.

Septic Diphtheria.—In diphtheria there are always associated with the specific micro-organisms streptococci and staphylococci in great abundance, and the latter often give rise to a concurrent septic infection which constitutes an important factor in the course of the disease. It is sometimes difficult to determine to what extent this secondary infection is responsible for results, as distinguished from those of the primary infection. Doubtless in many cases of diphtheria streptococcus infection is the principal cause of death.

Septic infection is most liable to occur in patients with intense nasal involvement, and in whose fauces the exudate assumes a dirty-gray or brownish appearance. Instead of becoming detached and peeling off *en masse*, the exudate breaks down into a semisolid or grumous mass. In such cases the decomposing and liquefying membrane gives rise to an offensive discharge from the nares and mouth, and a fetid breath. This discharge, ichorous in character, causes reddening and excoriation at the orifices of the nose and corners of the mouth, and the denuded surfaces are often converted into ulcers which quickly take on a dirty-gray coating. Sometimes there is considerable ulcerative action seen in the fauces and nares, but, strange to say, this process is commonly limited to the mucous membrane. It is only in rare cases that the subepithelial tissue is lost to a greater extent than would result from a small ulcer here and there. These ulcers are apt to remain covered for a long time with a yellowish coating.

The disorganization of the mucous membrane of the affected parts is commonly attended with capillary hemorrhages, more or less marked.

As might be supposed, the color of the false membrane is changed by its becoming infiltrated with blood. When the hemorrhages are copious, and the blood is poured out between the mucous membrane and the exudate, the latter is quite sure to be separated to a considerable extent. It is, therefore, not unusual to find in such cases a good deal of loose exudate in the throat, and in the nose also, undergoing rapid decomposition.

As the result of septic infection, the lymph glands of the neck become inflamed and swollen. The periglandular connective tissue may also inflame and swell to a certain degree. In some cases the swelling is so great that the neck is raised to an even line with the face. The skin becomes tense, smooth and shining, and may either feel doughy to the touch or as dense as a board. Suppuration may or may not result.

Attention has already been called to the fact that in septic cases a rash is apt to appear on the skin. The rash may at first be erythematous or slightly macular, but as the disease progresses it often assumes a petechial character.

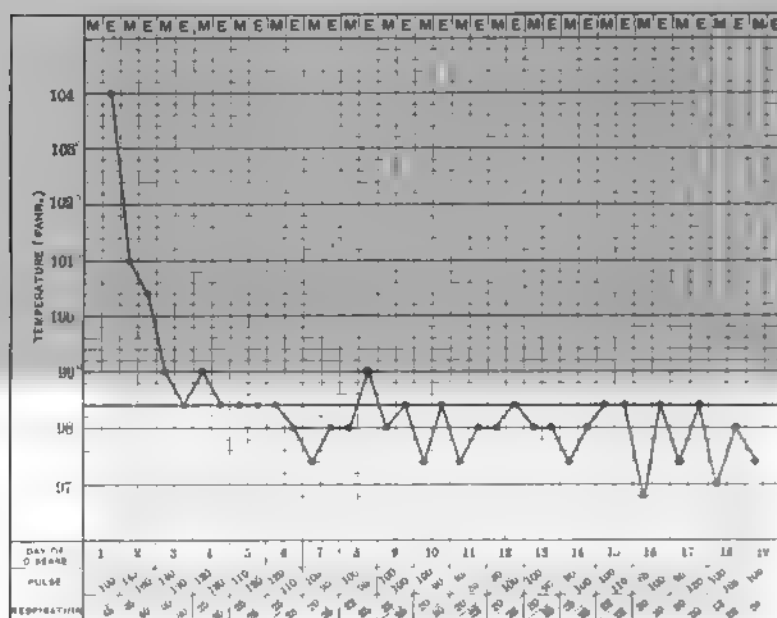
In this form of diphtheria the temperature runs comparatively high—

ranging from 102° to 104° F. There is usually considerable variation between the morning and evening records. The pulse is rapid and feeble, and the extremities are often cool. Suppuration of the middle ear is liable to occur, and pneumonia sometimes develops.

Children, restless at first, become apathetic later on, which condition increases until death supervenes. Death, however, is not the inevitable result, for the milder cases frequently recover.

Fever.—Except at the onset of diphtheria, fever is not a prominent symptom. The disease almost always begins with fever, more or less intense. In the milder cases the temperature of the body may not rise

FIG. 98



B. G., ordinary type of diphtheria, occurring in a child five years of age, showing a high initial temperature with a rapid decline.

much above the normal, but in the severer cases, during the first day or two of the disease, it usually ranges from 101° to 102° F.; but after the full appearance of the exudate—that is, after the second or third day—the temperature commonly drops to normal, and sometimes below. Our experience accords with that of Lennox Browne, who says: "Of 1000 cases which came under observation, on an average, on the third day of the diphtherial attack, the temperature in 80 per cent. was 101°; while in 50 per cent. the average temperature during its course was below 99°."

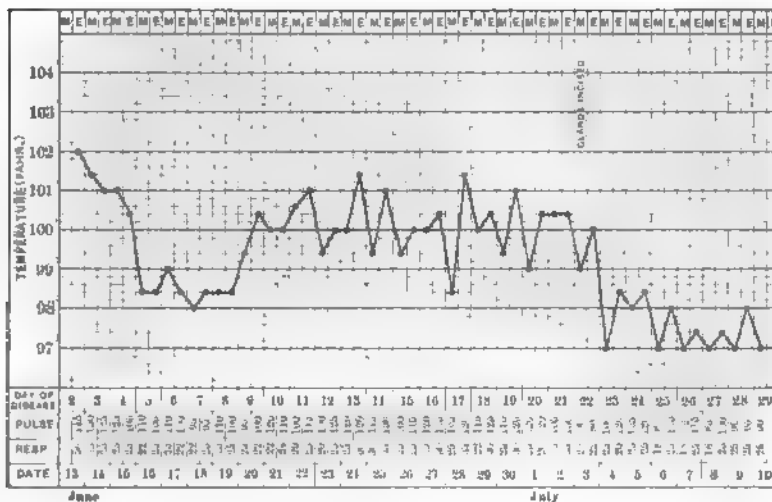
As already stated, the average temperature in the septic form of

diphtheria is always comparatively high, while in the toxæmic cases it falls to normal and even lower.

In acute adenitis, which often occurs as a complication in diphtheria, the temperature ranges high, sometimes to the extent of 104° to 106° F. If suppuration takes place and the pus is liberated the hyperpyrexia at once subsides. In every case of continued high temperature one should suspect the existence of some complication. The degree of fever, under such a circumstance, is usually not different from that which is characteristic of the associated disease.

What has been said of the temperature in ordinary diphtheria does not apply with equal force to the laryngeal form of the disease. In this class of cases, instead of falling after the first two or three days of illness, it frequently continues high, especially when intubation is required

FIG. 94



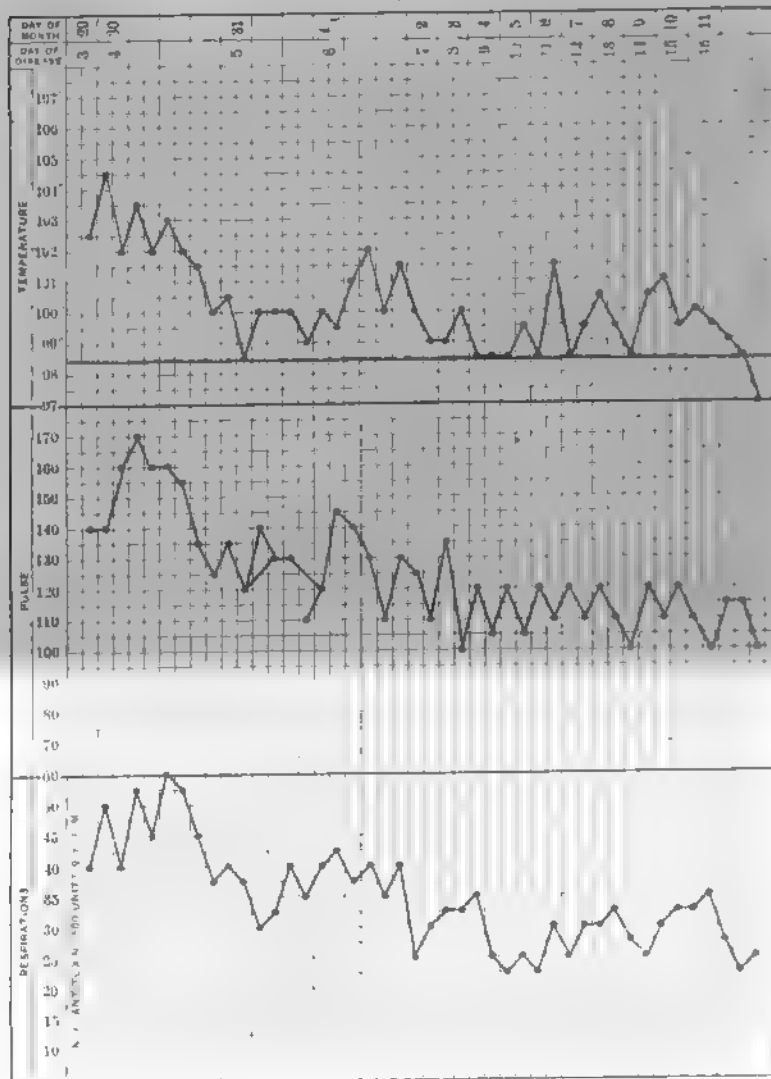
E. M., aged five and one-half years; septic type of diphtheria in a patient with copious exudate in the throat; swollen cervical glands, later suppurating. Recovery.

for relief of the stenosis, and while the tube is in the larynx. In the majority of such cases the temperature continues at 101° to 102° F. for a number of days. If bronchopneumonia develops, which is not an infrequent complication, the temperature will continue high for an uncertain length of time.

Circulatory Symptoms.—In all well-marked cases of diphtheria the pulse is frequent. Its rapidity, indeed, may be out of proportion to the temperature. In severe cases, especially in children, the pulse ranges between 120 and 160 per minute, and, as the disease progresses, becomes irregular and weak. The apex beat of the heart is often diminished in intensity and the first sound becomes indistinct. Attention has already been called to the fact that the action of the heart is greatly influenced by the profound asthenia resulting from toxæmia.

An abnormally slow pulse is of grave import, and will be referred to again when considering the question of prognosis.

FIG. 95



C. S., case of laryngeal diphtheria of average severity admitted to the Municipal Hospital on the third day of the disease, showing decline of temperature after removal of the intubation tube. Recovery.

The Urine.—In the milder cases no marked change is found in the urine, either in the quantity voided or its constituents. In severe cases it contains an excess of urea, and sometimes epithelial cells and casts. Hæmaturia is much less common than in scarlet fever. Albumin in

small quantities is found in a large proportion of cases. It is said to be present in about one-third of all cases; but this estimate is, according to our experience, much too low. Some writers believe that albumin is more often found since antitoxin has come into use. Suppression of urine and uræmic symptoms are rare. This subject will be referred to again when considering the complications of diphtheria.

Nervous Symptoms.—In the acute stage of diphtheria nervous symptoms are not a prominent feature of the disease. Convulsions sometimes occur as an initial symptom in children of nervous temperament. In fatal cases convulsive movements are not infrequent in the death struggle. Delirium occurs only in exceptional instances, and, when present, is usually mild. Children, as a rule, sleep well; they often, indeed, lapse into a state of apathy or stupor.

Paralysis of the palate is often seen during the acute stage, or, at least, before the exudate has entirely disappeared from the fauces. We have frequently noticed its presence as early as the seventh to the tenth day of the diphtherial attack. Its existence is manifested by slight difficulty in deglutition, and by a nasal tone of the voice. Also, at an early stage of the disease, the cardiac nerves may become involved, giving rise to cardiac syncope, which is a common cause of sudden death. General paralysis frequently occurs during convalescence. This will receive due consideration under the head of sequelæ.

Laryngotracheal Diphtheria, or Membranous Croup.—This form of diphtheria may be described as a pseudomembranous exudation into the larynx and trachea, giving rise to symptoms of croup. It owes its origin to the same specific cause that is operative in producing diphtheria of the fauces and nares, namely, the Klebs-Loeffler bacillus. Before this organism was discovered and definitely shown to be the material etiological factor of diphtheria exudation, it was pardonable to have considered membranous croup as the result of a non-specific laryngotracheal inflammation. It is certainly no longer permissible to speak of an idiopathic catarrhal croup, except as applied to a spasmodic affection of the larynx of an entirely different character. Catarrhal croup is quite free from danger, and non-contagious.

It must be admitted, however, that pseudomembrane may form in the larynx, as on the tonsils, from microbic causes in which the Klebs-Loeffler bacilli have no part. The streptococcus is the particular micro-organism found in this condition, and is believed to be responsible for the membrane, although the staphylococcus has been found as well. The symptoms caused by an exudation in the larynx due to these organisms are precisely the same as those caused by the genuine bacillary exudation. If differentiation be possible, it is only by the aid of bacteriological examination.

Our experience leads us to believe that an exudation into the larynx and trachea of streptococcic origin is rare. While admitting the possibility of such an occurrence, it is certainly safer, both for the patient and the public, to regard and treat all cases of membranous croup as genuine diphtheria.

Some authors teach that in diphtheria the exudation rarely occurs primarily in the larynx and trachea, believing that it invades these parts by downward extension. This is undoubtedly true of most cases, but we have frequently seen membranous croup in children whose fauces and nares were entirely free from membrane. Some of the worst cases are of this description. Our experience warrants the statement that in fully one-half of all cases there is only scanty exudation in the fauces. It is often seen only on the tonsils in the form of dots, but may present a scattered appearance on the adjacent parts. In many instances the exudation will be found at the outskirts of the larynx on the lateral glossoepiglottic folds. The epiglottis is frequently involved. Lennox Browne believes that the epiglottis is almost invariably first attacked, and seldom escapes. His experience leads him to believe that it is the rule, when the larynx is involved, for the exudation to begin on some parts of the fauces and extend downward.

While laryngeal symptoms often constitute the first evidence of diphtheria in children, there are many instances of the disease beginning in the fauces and nares and continuing for several days in a severe form before the larynx becomes involved. This has been called descending diphtheria. In this, and, indeed, every form of the disease, the exudation may extend into the trachea, the bronchi, and even into the bronchioles (Fig. 96).

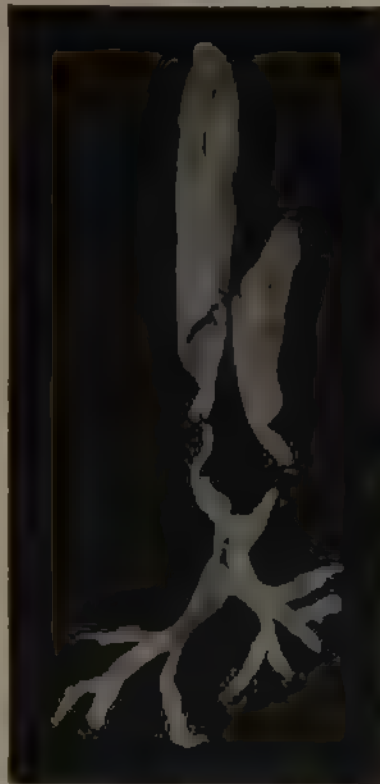
Cases of ascending croup have been described; that is to say, the exudation beginning in the bronchi has extended upward into the trachea and larynx. This cannot be proved, and it is doubtful whether it ever occurs.

Symptoms.—When diphtheria exudation invades the larynx, the symptoms vary somewhat according to the age of the patient. In children, in whom the lumen of the larynx is small, symptoms of impaired breathing soon appear. The symptomatology may be divided into three stages, according to the development of the disease. In the first stage the symptoms consist of cough and hoarseness, in the second of aphonia and dyspnoea, and in the third of suffocation and asphyxia, speedily ending in death if relief be not afforded. It must not be supposed that all three stages are seen in every case, for there are undoubtedly instances of abortive croup.

When the larynx is primarily attacked, the disease at first is often thought to be nothing more than a common cold; but as it progresses its real nature becomes apparent. There is always cough, more or less pronounced, and it soon becomes hoarse and high-pitched, with a shrill, metallic sound. Hoarseness and huskiness of the voice exist with some discomfort in the throat, and moderate fever. As the exudation increases the voice becomes less and less distinct, and often loses its sonorous character. Frequently, at an early stage of the disease, the symptoms do not prevent the child from getting out of bed and playing, even when there may be some evidence of beginning dyspnoea. In one, two, or three days marked disturbance of the respiration is noticed, often sufficient to cause grave apprehension. The obstruction of the

larynx, due to exudation and swelling, is sometimes increased by spasm of the laryngeal muscles. As the disease advances respiration becomes more and more difficult, until distressing dyspnoea supervenes. The inspired air is insufficient to fully expand the lungs, which is evident from the sinking in of the lower end of the sternum and the lower ribs at each act of inspiration. The blood is insufficiently oxygenated, as denoted by a livid hue of the skin. The child is restless, cannot sleep, constantly changes its position in bed, and vainly looks in every direction

FIG. 98



A cast of exudate expelled from the larynx and passages leading down into the subdivisions of the right and left bronchi. The cast extended from the larynx downward into the subdivisions of the right and left bronchi.

for relief. One does not often see a more pitiable sight than a little child suffering from well-developed membranous croup.

In describing these symptoms Lennox Browne truly says: "Each inspiration is attended by a peculiar stridor which constitutes one of the most marked characteristics of the disease. This stridor has been variously described as high-pitched, piping, shrill, metallic, sibilant, and wheezing. During the dyspnoea there is indrawing of all the muscles of the suprasternal and substernal regions, as also of the epigastrium, the false ribs, and even the lower portion of the sternum itself; of all those

parts, in fact, which would generally be distended in healthy inspiration. All the inspiratory muscles, regular as well as auxiliary, are observed during the spasm to work painfully; the dilated nostrils, the terrorized expression of the face, and convulsive movements of the limbs, all giving evidence of a laborious and futile struggle for breath. The complexion becomes cyanotic, and death from apnoea appears imminent, and may even occur. Should membrane be coughed up there may be a favorable termination to the dyspnoea, when the metallic sound of the cough will be observed to change to that of a bronchitis or remitting laryngitis."

Laryngeal diphtheria is by far less common in adolescent and adult persons, and much less fatal, because the danger from stenosis is not so great. The greater development of the larynx in persons of mature years permits of some diminution of its aperture without affecting seriously the respiratory act. We have, however, met with a few instances in which the mechanical obstruction was so great as to demand operative interference. When the exudation is limited to the larynx intubation will afford relief, but when the trachea is also involved tracheotomy is to be preferred.

In membranous croup the temperature is usually higher than in faucial diphtheria. While the intubation tube is being worn the temperature is liable to remain two or three degrees above the normal.

The laryngotracheal form of diphtheria has a decidedly local character, and is, therefore, not so liable to be attended with symptoms of systemic poisoning. Toxæmia and general paralysis are not often seen in this form of the disease when it is strictly localized. The infrequency of constitutional symptoms may be accounted for by the comparative absence or scantiness of lymphatics in the larynx and trachea. Apart from the stenosis, the principal source of danger in membranous croup is from capillary bronchitis or bronchopneumonia.

THE COURSE, DURATION, AND TERMINATION OF DIPHTHERIA.

In *mild cases* of diphtheria the local lesions are moderate in degree and the constitutional symptoms not serious. The exudation is scanty and limited to the tonsils. At the onset the temperature usually rises two or three degrees, sometimes a little higher, but quickly falls to near the normal. The mucous membrane of the fauces is congested, and deglutition slightly painful. There is usually loss of appetite and some prostration. The pulse rate is accelerated—the rapidity at times being out of proportion to the rise of temperature.

In this purely local form of the disease the height is reached in from two to four days, when all the symptoms begin to subside. The exudation disappears, and the small areas of superficial ulceration left behind rapidly heal. In from four to seven days the fauces assume their normal appearance, and the patient expresses himself as feeling well, although there is apt to be some loss of strength and anæmia. Sequelæ are extremely rare.

In the *severe type* of diphtheria the constitutional symptoms are

usually well marked from the beginning. The temperature runs up quickly to 102° or 103° F., there is loss of appetite, the throat is painful, and the child is restless and unable to sleep long at a time. Chilly sensations may be experienced, and occasionally convulsions occur.

When an early examination of the throat is made the mucous membrane will be found to be of a vivid-red color, with moderate swelling of the parts. The uvula soon becomes œdematous, elongated, and swollen. This inflammatory action does not continue long, perhaps only a few hours, until the exudate appears. In its earliest manifestation it presents the form of grayish or yellowish-white spots of pinhead size. These form into groups which quickly coalesce, and thus develop into large patches. In most cases the exudation is first seen on the tonsils and rapidly spread to other parts of the fauces. Frequently, in twenty-four to forty-eight hours it covers not only the tonsils, but the anterior pillars, the uvula, and a large part of the soft palate. With this increase of exudation the temperature, strange to say, often falls one or two degrees. The lymphatic glands of the neck, near the angle of the jaw, are almost always swollen.

In *favorable cases* the local symptoms reach their maximum development in forty-eight hours, and after remaining stationary for a day or two begin to subside. The exudation sometimes exfoliates in large masses, and at other times melts away little by little. When it becomes detached and peels off it may disappear entirely in from six to eight days, sometimes sooner; but when it melts away gradually, a longer time is required. The mucous membrane of the parts involved is left reddened, and shows superficial ulcerations. Often the uvula suffers the greatest loss of substance from the ulcerative action, as it is honey-combed, shrivelled, and tapers down to a small point. The ulcers usually heal rapidly. Simultaneously with the decrease of exudate the pulse becomes less frequent, and, in favorable cases, maintains fair volume and regularity. The swelling of the glands of the neck subsides, the appetite improves, and the patient is fairly on the road of convalescence. But even when recovery seems most probable, the physician in giving a prognosis should express himself with some reservation, for dangerous symptoms may yet follow, such as indicate toxæmia, heart-failure, or paralysis.

In *very severe cases* all symptoms are, of course, greatly intensified, and complications are much more liable to ensue. The exudation is usually copious, covering thickly the entire fauces, and is often seen extending forward on the vault of the mouth beyond the junction of the soft and hard palates, on which location it is apt to be especially thick.

It frequently travels backward to the pharyngeal wall, the postnasal space, and into the nares. It may even extend downward into the larynx and trachea.

As already mentioned, the local and constitutional symptoms do not progress *pari passu*. On the contrary, while the exudation is increasing the fever may diminish to such an extent that the body temperature is but little above the normal. The pulse rate, however, does not

always decrease proportionately, but may even grow more rapid. The appetite often improves, swallowing appears to be less painful, and not infrequently the general condition and strength of the patient seem improved, while the danger is in nowise diminished. The physician should be careful not to be misled by this apparent improvement while the disease is still progressing.

When diphtheria assumes the *septic form*, the secretion and exudation of the throat and nares undergo rapid decomposition, and, unless these parts are frequently cleansed with antiseptic washes, there is emitted with the breath a peculiar odor which is in the highest degree offensive. This odor is often so foul as to suggest the existence of gangrenous destruction of the tissues, and yet the disorganization of the parts rarely amounts to more than a superficial ulceration. Coincidentally with this condition, the cervical and submaxillary glands, usually somewhat swollen from the beginning, greatly increase in size by inflammatory action, which also involves the adjacent cellular tissue. While abscesses frequently form, yet it is surprising how rapidly this swelling will often subside without abscess formation as soon as the throat symptoms show signs of improvement.

In *septic cases* the fever, instead of diminishing in two or three days, as in the other varieties of diphtheria, continues, or may even increase, until the throat and nose symptoms improve and the swelling of the neck subsides. Recovery may take place from this form of the disease, but the majority of patients die. Death often occurs at an early stage, as early as the fifth to the seventh day, from extensive systemic poisoning due to a mixed infection. Sometimes the poisoning is more gradual, in which case the exudate disappears, the glandular swelling subsides, and the temperature falls, but instead of improving the patient remains apathetic, loses weight, becomes anæmic, grows weaker and weaker, and gradually passes away. A not uncommon cause of death is pneumonia of septic origin.

The presence of epithelial and hyaline casts in the urine, together with a large amount of albumin, points to a rapidly developing systemic poisoning, and may often prove to be an early monitor of danger.

When recovery takes place from the septic form of diphtheria convalescence is usually very slow, often, indeed, extending through many weeks. The symptoms of septicæmia become less and less marked, and prostration gradually gives way to general improvement. But in the fourth or fifth week of the disease, even after an apparent recovery, some late complication, more especially general paralysis, is extremely liable to set in. This is true not only of the septic form, but of all well-marked cases of diphtheria. The vast majority of patients recover from the paralysis, but it is sure to prolong the period of convalescence for weeks or even months.

In the *malignant type* of diphtheria the earliest symptoms give marked evidence of systemic poisoning. By the time the false membrane has formed, which is usually in twenty-four to forty-eight hours, the whole organism is profoundly affected. The membrane covers thickly

PLATE LVIII.



THE QUEEN OF SHEBA

1577

the entire fauces, often involving the nares also; the breath is fetid, the saliva dribbles from the mouth, blood oozes from the nose, and purpuric or petechial spots appear upon the skin; the glands of the neck and the periglandular tissue are greatly swollen; the face is bloated, pale, and waxy in color; the temperature is either slightly elevated or subnormal; the pulse may be rapid and feeble or slow and irregular, and the intellect, clear at first, soon becomes clouded. Death in these cases may occur in forty-eight hours, and is rarely delayed longer than three or four days.

The course and duration of *membranous croup* vary in different cases, according to the extent of the disease. In mild cases the symptoms often disappear in a few days under ordinary treatment, without operative interference. When the larynx is involved to the extent of causing stenosis, death is sure to result speedily if relief be not afforded. If the exudation is limited to the larynx the obstruction to respiration is almost always overcome by intubation, and in the course of six or eight days the patient may be considered comparatively free from danger, at least so far as the primary trouble is concerned. But when the exudation extends into the trachea, intubation may give relief at first, though death is liable to occur a few hours later. Death commonly results when the disease extends into the bronchi and bronchioles. It occurs through insufficient decarbonization of the blood, due to the mechanical obstruction caused by the false membrane and retained secretions in these parts.

In cases which linger longer the fatal result may be brought on by collapse of certain parts of the lungs to which the air does not have access, or by the development of capillary bronchitis or bronchopneumonia. Many patients develop the latter affection when they are believed to be well on the way to convalescence. This, indeed, is one of the principal causes of fatal termination in laryngotracheal diphtheria.

When membranous croup is likely to terminate in recovery, improvement begins with a decrease in the fever and an abatement of the laryngeal symptoms. The false membrane usually disappears in from four to eight days. Sometimes it is coughed up in cylindrical or irregular casts, but more often it disappears gradually, probably by being liquefied and expectorated; it is quite impossible to believe that it ever undergoes absorption. When thrown off in casts it is liable to reform, and when such new formations take place the disease is apt to terminate fatally. In patients that recover, hoarseness or aphonia, and often some difficulty in swallowing, continue for a longer or shorter time after the intubation tube has been removed. This change in the voice, according to Oertel, is to be ascribed to a flaccid condition of the vocal cords and atony of the laryngeal muscles.

RECURRENCE OF DIPHTHERIA.

Many authors believe that a second attack of diphtheria seldom occurs in the same individual within a short space of time. While this may be accepted as the rule, yet it must be admitted that there are many exceptions. It is certainly true that a person who has survived the disease does not have conferred upon him for any considerable length of time that immunity which is so characteristic of scarlet fever, measles, and smallpox.

We have quite often readmitted children to the hospital with recurrent diphtheria within a few months from the previous attack; and in two or three instances, at least, children have returned with a third attack. Quite often also have we seen patients suffer from a relapse of the disease before leaving the hospital. In such instances, after the subsidence of all constitutional symptoms and the complete disappearance of the membrane, the patient, during convalescence, is seized with a sore throat, the temperature rises, the glands of the neck become swollen and sensitive, and the exudation recurs in the throat, or nares, or both.

The relapse is not, as a rule, so severe as the primary attack, but there are some exceptions. We have more than once seen death result from a recurrence of the disease.

COMPLICATIONS AND SEQUELÆ OF DIPHTHERIA.

Heart.—The poison elaborated by the bacilli of diphtheria is especially prone to affect the heart. In all severe cases heart-failure is extremely liable to occur. Symptoms of this condition may appear before the pseudomembrane has entirely separated, but in most cases they are not apparent, or, at least, do not become prominent, until the characteristic feature of the local affection has, to a great extent, disappeared. In other words, signs of cardiac failure are rarely seen until the diphtherial process has made considerable progress. They do not often appear before the end of the first week, but during the four or five succeeding weeks the patient is in constant danger of heart-failure.

It is believed by some authors that the heart is affected to a greater or less degree in all cases of diphtheria. Jacobi¹ says: "There is no case ever so mild apparently that will not affect the heart's function at once to a certain extent. From mild cases to the gravest there are gradual transitions." In a large proportion of the severe cases which survive long enough the myocardium shows (post-mortem) certain anatomical changes, the most common of which is fatty degeneration.

Undoubtedly, heart-failure not infrequently results from paralysis of the cardiac nerves, and quite independently, too, of any anatomical change in the heart muscle. Lennox Browne credits Vincent, of Paris, and P. Meyer with having found "widespread parenchymatous changes

¹ Twentieth Century Practice of Medicine.

in the cardiac plexus in two cases of patients dying of heart-failure during convalescence from diphtheria, in which the heart muscle was unaffected." He says: "The changes were exactly similar to those found in the peripheral nerves in ordinary postdiphtheritic paralysis."

The *symptoms of heart-failure* do not differ from those of toxæmia. Vomiting is often an early sign. The patient is pale and sallow, sometimes livid and cyanotic; the pulse at first may be rapid and feeble, but soon becomes slow, irregular, and intermittent, or dicrotic. The pulse rate is frequently as slow as 40 to 50 per minute. The first sound of the heart grows less distinct. The circulation is sluggish, and the extremities are cold, but the mind remains clear. In severe cases, as the end approaches, the pulse becomes absolutely lost at the wrist, and death results gradually from asthenia, or it may result suddenly from heart-failure. Undoubtedly death sometimes occurs from paralysis of the cardiac plexus. Recovery but seldom takes place after the symptoms of heart-failure once assume a threatening character.

Lungs.—In faucial diphtheria the lungs do not very often become affected. Bronchitis occasionally occurs, as does also bronchopneumonia. But in the laryngotracheal form of the disease these complications are extremely common. Indeed, bronchitis, more or less marked, is not very often absent in membranous croup. As the inflammation extends downward from the laryngotracheal surface to the bronchi, the inflamed mucous membrane is apt to become involved in the diphtherial process. But quite apart from this, bronchopneumonia, catarrhal in character, is of frequent occurrence, and constitutes one of the principal sources of danger. It most often sets in before the acute stage of membranous croup has passed, but it may occur at any period following this stage, even during convalescence. J. Lewis Smith says: "In 121 cases of bronchopneumonia complicating diphtheria, observed by Sanné, the pneumonia commenced in 2 on the first day of diphtheria, and in 71 between the second and sixth days inclusive."

When it develops at a later stage, or during convalescence, it is in most cases preceded by a mild bronchitis that has never entirely disappeared.

The existence of a bronchopneumonia is revealed by physical examination. Both lungs may be found involved, although the disease is usually better marked in one than in the other. The physical signs may show that the inflammation is limited to the lower lobes, but more frequently disseminated areas of inflammation are found throughout one or both lungs.

As already stated, bronchopneumonia is one of the chief sources of danger in diphtheritic croup. The mucopurulent material secreted in the bronchial tubes may be so abundant as to clog the tubes and prevent proper decarbonization of the blood. As the inflammation extends to the smaller tubes, these often become clogged in the same way so as to prevent the entrance of air to the alveoli, which gradually collapse. Autopsies often reveal areas of atelectasis disseminated throughout the lungs. Even where the tubes remain pervious it is almost impossible

for the child to expectorate the mucopus on account of its viscosity. Hence, the minuter tubes are usually found (post-mortem) to be filled with a thick, viscid material, containing also not infrequently floating particles of pseudomembrane.

Bronchopneumonia is always attended by an elevation of temperature. The disease may either run an acute course, terminating in recovery or death in six to eight days, or assume a subacute form and continue to progress for two, three, or more weeks. In some of these persistent cases recovery finally takes place, but more often death results from exhaustion. Bronchopneumonia is the chief cause of death after tracheotomy.

Lobar pneumonia is not a very frequent complication. It has been known to occur during the stage of convalescence. Areas of consolidation in the lungs are not infrequently seen, but they are almost always associated with inflammation of the bronchi.

Pleurisy does not very often occur as a complication. According to J. Lewis Smith, "Peter found the lesions of pleurisy 9 times in 121 autopsies in diphtheria, and Sanné observed them in 20 cases." The latter is quoted as saying that pleurisy always accompanies some other phlegmasia. In our experience in the hospital we have not seen more than two or three frank cases of pleurisy attended with pleuritic effusion.

Lymphatic Glands.—Enlargement of the cervical and submaxillary glands is of common occurrence in diphtheria. It may be either slight or excessive. In septic cases this complication is usually most marked. As already stated, the inflamed glands sometimes break down into abscesses.

Kidneys.—Renal complication occurs earlier in diphtheria than in scarlet fever. Albuminuria is frequently seen as early as the third or fourth day, sometimes even on the second, while the quantity of urine is not diminished, but may be increased. It is believed that the elimination of the toxin with the urine irritates the kidneys, and thus tends to affect their function or even damage their parenchymatous structure. In cases showing albuminuria the kidneys may be found to be normal, or they may exhibit various degrees of parenchymatous inflammation. While acute nephritis is not so common as in scarlet fever, yet it does occur. This is evident from the fact that hyaline and granular casts are sometimes found. Red blood cells are rarely present. The urine in such cases is diminished, sometimes scanty, and the skin becomes pallid. Oedema is less pronounced, and uræmic symptoms are much less frequent than in postscarlatinal nephritis. Still patients die now and then from uræmia. According to Jacobi, "When albumose is found, together with considerable albumin, Berlin believes the prognosis to be rather favorable. Still, in most of the cases at the clinic at Strassburg in which he made his observations, the renal complications were only trifling."

Park¹ says that in most severe cases of diphtheria the kidneys are in

¹ Loums Thompson, *American System of Practical Medicine*.

a state of more or less acute nephritis; that they are usually hyperæmic and enlarged; that the surface of the kidney is smooth, and frequently the seat of small hemorrhages, and that, microscopically, the signs of marked parenchymatous changes are evident up to complete necrosis of the epithelium lining of the tubules. "In severe cases the urine contains abundant albumin, degenerated kidney epithelium, leukocytes and hyaline casts, and, in the most severe, coarse and fine granular casts. Blood cells are infrequent."

Lennox Browne believes that there is a decided tendency to renal complications in all cases intoxicated with the diphtherial poison. In a series of 1000 cases of diphtheria tabulated by him he found, however, that the mortality due to nephritis and its results was only 2.7 per cent. This is a much larger rate than was observed in all the Metropolitan Asylums' Board Hospitals in 1893, when, he says, out of a total of 2848 cases of diphtheria treated, with 865 deaths, only 8 cases of nephritis were reported. But while actual nephritis does not occur with great frequency, yet, as already stated, the parenchymatous structure of the kidneys is very commonly damaged to an extent that interferes with their proper function. Lennox Browne says albumin in some quantity is to be found in the urine in fully one-half of the cases of true diphtheria. Some other observers state that it is present even in a much larger proportion of cases, and believe, with Lennox Browne, that it is more frequently seen since the serum treatment has been employed. When it is present to the extent of more than one-eighth of the volume of urine, the amount of urine secreted is apt to be diminished, and uræmic symptoms may appear.

As to the frequency of albuminuria in diphtheria, J. Lewis Smith says: "Bouchut and Empis found it in two-thirds of their cases, Germain Sée in one-half of his, and Sanné in 224 cases out of 410. In New York City, where diphtheria has been many years naturalized or endemic, I made, in the years 1875 and 1876, daily examinations of the urine in 62 consecutive cases, and found it present in 24, while 38 were recorded exempt. But the proportion of cases as stated in my statistics is probably below the truth, for the albuminuria is sometimes transient and it often occurs as a mere trace and is liable to be overlooked. Its duration is frequently not more than from one to three days, and in the majority of instances it does not continue longer than ten days; but we are all familiar with cases in which it continues fifteen or twenty days, or even months."

As the amount of albumin in the urine varies in different patients, so also does the day of the disease on which it makes its appearance vary. In referring to Sanné's observations on this point J. Lewis Smith says: "In 224 cases albuminuria was detected on the first day of diphtheria in 3, on the second day in 10, on the third in 30, on the fourth day in 30, on the fifth day in 32. From the sixth day to the eleventh the number on each day in whom albuminuria was present for the first time varied from 10 to 33. After the eleventh day there were only 9 new cases, and after the fifteenth day only 1 new case. Hence, from

these statistics we infer that there is little danger that albuminuria will occur after the second week, if the patient has exhibited no symptoms of it previously."

In examinations of the urine made under our direction of 149 diphtheria patients in the Municipal Hospital, albumin was found to be present in 85 per cent. of the cases. The cases were not selected, but taken consecutively as they were admitted to the hospital in two different periods of time. The observations, therefore, include both mild and severe cases of diphtheria. The first series of examinations comprised samples of urine from 37 patients, and the second from 112 patients. Of the former, 73 per cent. of the cases showed albumin, and a few showed tube casts also. The urine was not examined in all cases as frequently as we desired, for the reason that most of the patients were young children from whom it was often impossible to obtain specimens. But in no case were there less than two examinations, and in some as many as twelve. In most of the patients that recovered the urine became normal during convalescence, but a few still showed a trace of albumin when discharged from the hospital.

Of the second series of examinations pertaining to the urine of the 112 patients, albumin was found in 90 per cent.; 20 per cent. of these cases showed albumin in large quantity, and 70 per cent. in a less amount—not more than a trace being found in some.

In 24 patients showing a large amount of albumin the urine was examined microscopically, and tube casts, hyaline and granular, were found in 2 of this number. We should add that 1 of these patients had nine months previously suffered from scarlet fever, and we had no knowledge of the condition of the urine since then.

Strange to say, in a few of the fatal cases in which the kidneys were examined *post-mortem* there was macroscopic evidence of parenchymatous changes, although examination of the urine had failed to show tube casts of any description.

Scarlet Fever.—Scarlet fever is not an uncommon complication in diphtheria; or, more properly speaking, one of these diseases is often found associated with the other. We venture to say that anyone who has had experience in a hospital for contagious diseases will bear out this statement. Being familiar with the experience of, at least, two or three such hospitals, we know how frequently scarlatinal rashes are found in the diphtheria wards, and, on the other hand, how often diphtheria appears in the scarlet-fever wards. For the past two years we have been in the habit of examining (bacteriologically) the throats of all scarlet-fever patients as soon as they are admitted to the hospital. In dividing these examinations into series of 100 cases each, the Klebs-Loeffler bacillus has been reported present by The Bacteriological Division of the Bureau of Health, Philadelphia, in from 10 to 33 per cent. of the patients. Some showed well-marked clinical evidence of diphtherial complication, while in others, it must be said, such evidence was not apparent. It is not uncommon to admit to the hospital patients in whom these diseases coexist in a well-pronounced form.

Lennox Browne quotes Dr. Bruce Low as saying that "during the prevalence of diphtheria in Hastings the two diseases in certain instances were concurrent, and in a number of persons who, on account of their suffering from scarlet fever, were sent to the borough sanatorium for isolation and treatment, were attacked by well-marked diphtheria during their convalescence," giving also several examples "of importation of diphtheria into families by members returning home from the sanatorium after recovery from scarlatina, the patients in each instance not having been known to suffer from diphtheria during stay in the hospital."

In many cases of diphtheria with concurrent scarlet fever it is impossible to explain the source of the double infection. In hospitals for contagious diseases it is sometimes felt that one disease is engrafted upon the other through exposure to the second infection; but in private families these diseases not infrequently coexist without any known or explicable cause. One of the writers has just witnessed an instance of this kind in which two children of a family of three took scarlet fever; subsequently an infant of eleven months, who had not been out of the house for some time, fell ill with the disease and in two or three days developed also symptoms of severe diphtheria. Copious exudate appeared in the fauces and nares, and death quickly ensued from systemic poisoning.

Measles.—The relation of measles to diphtheria is a matter that has not received as much notice by writers as its importance deserves. Ryland referred to it in his Jacksonian Essay in 1837, and Dr. West in 1843. A few other observers have called attention to the fact that in times of concurrent epidemics of diphtheria and measles, subjects of the latter disease frequently suffer also from the former. In reporting on an outbreak of diphtheria in 1894 at Barnham Broom, England, Mr. T. W. Thompson says: "I find from my notes that with one or two exceptions, all the children, who later suffered from diphtheria, had about this time suffered from measles, which in some cases had been attended with considerable soreness and external swelling of the throat. The frequency with which diphtheria is found to coexist with or quickly follow in the wake of measles is such as to suggest a relationship between the two phenomena; though the relationship may be of an indirect kind only, the measles increasing susceptibility to diphtheria, mainly, in all likelihood, by the damage inflicted on the mucous membrane of the throat." There is no doubt that the catarrhal inflammation of the upper air passages incident to measles affords a fertile soil for the propagation of diphtheria bacilli.

The occurrence of measles with diphtheria should be regarded with great apprehension. The diphtheria is liable to assume the laryngo-tracheal form, and the development of bronchopneumonia is to be feared. In the year 1900 measles of an unusually severe type broke out in the diphtheria wards of the Municipal Hospital, and in all 68 cases came under our observation. Of these 34 died, making the death rate 50 per cent. Of the 68 cases, 34 developed membranous

croup, and of these 29 died—a death rate of 85.29 per cent. Bronchopneumonia was the principal cause of death, though some sank and died in a state of adynamia.

Paralysis.—Paralysis might be regarded with much propriety as a symptom of diphtheria, but as it is not seen until the acute stage is passed, and more often during convalescence, we have preferred to consider it as a complication or sequela. Very little seems to have been known of diphtherial paralysis prior to the latter part of the sixteenth century. Nicholas Lepois called attention to it in 1580, and Miguel Heredia in 1690. According to J. Lewis Smith, Ghisi, of Italy, in describing an epidemic which occurred in 1747-48, when his own son had paralysis in a severe form following diphtheria, says: "I left to nature to cure the strange consequences, . . . which had been remarked in many who had already recovered, and which had continued for about a month after recovery from the sore throat and abscess. During this period this child spoke through the nose, and food, particularly that which was least solid, returned through the nares in place of passing down the gullet." About the same time (in 1748) Chomel, of France, described two cases of paralysis following what he called gangrenous sore throat. In 1771, Dr. Samuel Bard, of New York, described the symptoms seen in a little girl of two and a half years who had recovered from "Sore Throat Distemper," as follows: "Whenever she attempted to drink she was seized with a fit of coughing; yet she was able to swallow solid food without any difficulty. She improved, but in the second month she could scarcely walk or raise her voice above a whisper."

For the next fifty years and more but little is said of diphtheritic paralysis. This sequel must either have been overlooked, or regarded as a coincidence, or else diphtheria at that time was of so mild a type that paralysis did not often result. It appears that Bretonneau had not yet observed this sequela at the time of his first publication on diphtheria in 1826. It is said by J. Lewis Smith¹ that Bretonneau "did not recollect that he had seen a case of diphtheritic paralysis prior to 1843. Although a close observer of diphtheria, the paralysis had not been observed by him, or at least had not attracted his attention, until it occurred in the person of his townsman, Dr. Turpin, in 1843." From this time on, until his second publication appeared, in 1855, he saw a sufficient number of cases to convince him that this sequela occurs not infrequently, and called attention to it in his paper of the latter date. Since then nearly every writer on diphtheria has described this peculiar form of paralysis, and its frequent occurrence is an accepted fact.

Paralysis does not often follow mild tonsillar diphtheria. But when the soft palate and especially the nares are involved, partial or complete paralysis, not only of the muscles of the parts covered with exudate, but also of the entire muscular system is liable to occur. General paralysis does not appear immediately after the local evidence of diphtheria has

¹ Keating, *Cyclopedia of the Diseases of Children*.

disappeared, but develops gradually and slowly. The parts earliest affected are the soft palate and the pharynx, while the upper and lower extremities show this symptom later. From the slow development of the affection it seems probable that at first only a few fasciculi are incapacitated, and that gradually more and more of these become involved until the affected muscles are no longer under the control of the will. Paralysis is sometimes observed in the muscles of the eyes, the trunk, the bladder, the rectum, and the diaphragm. In most cases the paralysis is incomplete, but in rare instances it progresses to such an extent that the entire muscular system becomes incapacitated.

The cause and pathology of the paralyzes are not fully understood. It seems probable that the condition is due to a toxic neuritis involving the peripheral nerves, causing an interruption of the nerve supply to the muscles involved. It is said that the neuritic change may extend the entire length of the nerves, from their periphery to their origin, not only of the spinal but also of the cranial nerves.

It may be that some of the fasciculi of the enervated muscles undergo fatty degeneration, as this change has been seen in the myocardium. Anatomical changes have been found in the spinal cord, apparently resulting from myelitis. S. G. Henschn has reported a case of acute disseminated sclerosis of the cord with neuritis. Some writers believe that changes of this nature contribute an important part in the production of the paralysis.

Hemiplegia is but rarely seen in diphtheria. Only 2 cases have come under our observation. One case has been reported by J. W. Brannan. This writer is quoted by Jacobi as saying: "There are 35 cases in all recorded in medical literature of postdiphtheritic paralysis of cerebral origin. Six cases have come to autopsy; in 1 of these a hemorrhage was found in the internal portion of the lenticular nucleus, with destruction of the neighboring part of the internal capsule. In the other 5 cases there was embolism of the Sylvian artery. . . . In the total 35 cases there was complete recovery in 4, death in 7; and in all the others there was permanent paralysis of greater or less extent."

In studying the causes of diphtheritic paralysis Trousseau felt that the explanation of this symptom is beyond our comprehension and will probably never be known. Realizing the insufficiency of any one theory to explain all cases, Jacobi, in his renowned treatise on diphtheria, says: "It may be positively asserted that diphtheritic paralysis does not in every case depend on one and the same cause."

The frequency with which paralysis follows diphtheria depends upon the character of the epidemics. It occurs, of course, much more frequently in severe attacks than in mild attacks of the disease. According to Lennox Browne, in 2848 cases of diphtheria treated at the various Metropolitan Asylums' Board Hospitals of London, in 1893, it was noted in just 14 per cent. This proportion, he says, agrees in the main with that deduced from his own table of 1000 cases of diphtheria. While we have no data at hand of our own experience on this point,

we believe that at least 14 per cent. of our patients developed paralysis more or less marked.

Since paralysis develops very gradually and slowly, it is not always easy to determine at which stage of diphtheria it begins. The difficulty is increased from the fact that most of the patients are young children in whom the affection is usually not discovered until the more characteristic symptoms have appeared. However, it has been found from careful observation that paralysis of certain muscles, the palatal, for example, may occur in the acute stage, or, at least, immediately after the disappearance of the pseudomembrane. But the later manifestations, as seen in muscles remote from the fauces, especially in those of the extremities, diaphragm, etc., are more serious, and usually do not appear in a pronounced form until after an interval of more than four weeks from the commencement of the diphtherial attack. We cannot better illustrate our experience with this affection than by quoting J. Lewis Smith's account of two cases reported by Holt: "A child, aged two years, had diphtheria in August, and a second attack in the middle of October. She convalesced slowly, and in her convalescence had no paralytic symptoms, except a nasal voice, until December 1st, when multiple paralysis suddenly developed. A brother of this patient also had diphtheria in October, moderately severe, and early in convalescence paralysis of the muscles of the palate began, followed by that of the other muscles; but it was not until the middle of December that the lower extremities were paralyzed." J. Lewis Smith very properly adds "These cases are examples of the usual mode of commencement and extension of the paralysis."

While this sequela is not so often seen after the mildest attacks of diphtheria, at least not to any marked degree, yet instances have been recorded in which paralysis has occurred in persons who, presumably, were infected with the diphtherial poisons without having exhibited any of the ordinary symptoms of the disease. According to the author just quoted, Dr. Boissarie¹ has related cases of this kind which are remarkable, if not indeed unique. He says an officer of the police force, after ailing for two or three days, had a nasal voice, and, in attempting to drink, the liquids returned through the nose. The velum palati was found insensible and motionless, but the fauces were otherwise apparently normal. "In the hospitals alongside the barracks in which the above case occurred, a young man without fever, redness, or swelling of the fauces, had also a nasal voice, and return of liquid food through the nose. The porter of the hospital was similarly affected, and the doctor stated that certain other patients in like manner presented symptoms of paralysis, without the history of an antecedent diphtheria. Dr. Reynaud, called in consultation, expressed the opinion that the paralysis had a diphtheria origin; and this opinion was strengthened by the occurrence immediately afterward of an epidemic of diphtheria in the place where these cases occurred." J. Lewis Smith follows

¹ Gazette hebdomadaire, 1881

the account of these unique cases with the pertinent remark that it is probable an antecedent diphtheria had occurred of so mild a form as to have escaped notice.

The paralysis, as a rule, affects principally the motor nerves, although the sensory nerves are not infrequently involved also. Anæsthesia of some parts, particularly the fauces, has been observed, and tingling and numbness are sometimes felt in the extremities. The sense of taste has been known to be affected. Paralysis of the sensory nerves may be quite local, and is not seen until a somewhat later period than the motor paralysis.

As the symptoms and course of diphtheritic paralysis vary according to its location and muscles involved, it seems most convenient to speak of the clinical manifestations of its various forms separately.

Paralysis of the *palate* is often seen at an early stage of the disease. It may be observed as soon as the exudate has disappeared, or as early as the tenth day of the diphtherial attack. The first evidence is manifested by a nasal tone of the voice. This results from dropping of the soft palate, causing the air to escape through the nose in the act of speaking. There may be slight difficulty in swallowing, enough to make it necessary for the patient to drink cautiously. Later, in the third or fourth week, or after convalescence has actually set in, the deglutition may become more difficult, so that fluids, instead of being easily swallowed, regurgitate in large part through the nares, while some run down the larynx, causing cough and sometimes pneumonia. As already mentioned, *anæsthesia* is associated with this form of paralysis and adds to the difficulty of swallowing. In infants starvation may occur through their inability to suckle. Even in older children, and in adults also, when general paralysis of an extreme form develops, deglutition often becomes impossible, and death from starvation may result if feeding through an oesophageal tube be not resorted to.

When paralysis of the palate has continued for a week or two, faulty accommodation of the *ocular* movements may be seen. Most frequently the paralysis of the ciliary muscles is bilateral. The most common variety of axis deviation met with is convergent strabismus, resulting from paralysis of the external recti muscles. *Diplopia* is not of infrequent occurrence.

Slight *facial paralysis* occasionally occurs. It has been noted as appearing soon after the acute stage. We have seen but very few such cases, and in these the affection was unilateral.

Paralysis of the *cardiac* and *respiratory nerves* may appear any time after the first week of the illness. The exudate may have disappeared, more food is taken, the patient appears to be gradually improving, and the members of the family are cheerful at the prospect of a speedy recovery, when suddenly the scene changes. The heart action becomes weak, the pulse feeble, slow and irregular, sometimes rapid, the respirations superficial, and the patient becomes pale, often slightly cyanotic. Severe precordial or epigastric pain is often complained of in cases of sudden heart-failure. In the more favorable cases improvement may

follow active stimulation, and the patient may eventually recover. But too often the improvement is only temporary, for the heart-failure is liable to return after a few hours, or a day or two at the most, causing sudden and, to the inexperienced physician, unexpected death. There is no other disease in which symptoms of heart-failure occur so suddenly and unexpectedly, and there is perhaps no other disease in which physicians are so often deceived in the matter of prognosis.

Involvement of the *respiratory nerves* leads to paralysis of the diaphragm and sometimes pulmonary collapse.

General paralysis does not make its appearance until a very late stage of diphtheria. It is not often seen earlier than the fourth week, and may occur later than the sixth week. In most cases it appears between the fourth and sixth week. In almost every instance it is preceded by well-marked palatal paralysis, sometimes by loss of function of the muscles of the eye, especially those presiding over motion and accommodation. As a rule, the loss of power is first noticed in the lower extremities. This may increase until the limbs, especially the lower limbs, are rendered entirely useless for weeks.

The comparative immunity of the fingers in many cases may be mentioned as a peculiarity. Paræsthesia or anæsthesia, however, is frequently noticed in the fingers, palms of the hands, and feet. The degree of paralysis is not the same in all muscles; in some it is complete, while in others it is only partial. When there is complete loss of power in the lower extremities it is not unusual to find that the patient has considerable use of the upper extremities. The muscles of the *trunk* are often partially paralyzed, but only rarely is there loss of sensation. In general paralysis the *diaphragm* is often affected, but rarely to the extent of seriously interfering with respiration. Its involvement is more apparent in the act of *coughing*. In this act, instead of the sudden expiratory explosion, the *cough* is slow and straining, and apparently attended with some effort on the part of the patient. But paralysis of the muscles of the pharynx, preventing complete closure of the glottis, may have more to do in causing this peculiar symptom than paralysis of the diaphragm.

As J. Lewis Smith very truly says, even where the paralysis seems to be general there are groups of muscles which entirely escape. He, therefore, prefers the term *multiple paralysis* to that of *general paralysis* to designate this form of the disease.

Of the internal and visceral muscles liable to become involved, paralysis of the *diaphragm* or of the *heart* is of the most serious import, as it may be responsible for sudden death.

The *bladder* is sometimes involved, but rarely to any marked degree. We have never found it necessary to catheterize a patient to relieve this viscus, nor have we ever observed any loss of power in the sphincter muscles. Paralysis of the muscles of the *lower bowel* and *rectum* is said to occur at times, giving rise to constipation, but not affecting the sphincters.

The *ensemble* of symptoms of general or multiple paralysis is very

graphically described by Dr. C. W. Fallis in the *Medical Summary*, January, 1888. Dr. Fallis was so unfortunate as to have suffered from an attack of diphtheria which was followed by paralysis. The description he gives of his own case is as follows: "About three weeks after the subsidence of the disease the paralytic symptoms began to show themselves. Impaired vision was the first trouble noticed, inability to accommodate the eyes to near objects, and in taking up the paper to read one morning I found that I could scarcely see a word, and soon after, although distant objects could be seen as well as ever, high-power glasses were required to read any kind of print. Double vision was noticed afterward. At about the same time numbness of the tongue was felt, the muscles of deglutition became paralyzed, so that swallowing was attended with strangling and regurgitation of food through the nose. There was a rapid pulse, 120 to the minute, showing that the pneumogastric was involved. Weakness of the limbs, causing a staggering gait, appeared; fingers became weak and numb, so that small objects could not be picked up, the symptoms becoming worse and worse as the disease progressed. The muscles of the left side of the face became affected with all the symptoms of facial paralysis from organic disease. Motion became more and more impaired, till I could neither stand nor walk, and when at the worst I was perfectly helpless, could not feed myself, had to be lifted from chair to chair, turned in bed, and could not even lift my hand to my head, or throw one limb over the other. Sensation was so impaired that hands and feet felt like lifeless weights, and in the dark I could not tell whether my feet were on the floor or not. The muscles of respiration were at no time affected to such an extent as to render breathing difficult, and the power of perfect speech was retained. Paralysis of the bowels necessitated the use of warm-water injections to promote their action. Some of the symptoms abated, while others became more aggravated, those first to appear being generally the first to subside; however, the smaller-sized muscles recovered rapidly, while the large, fleshy ones were more tardy in reaching their normal state, the facial paralysis lasting but a few days, while locomotion was either labored or impossible for weeks. The course of the disease from the beginning to the worst stage was about nine weeks, when it remained stationary for two weeks. Improvement was at first very slow and tedious, but after I could walk a little it was much more rapid, and by the fifteenth week, with the exception of some weakness, I was well."

We have seen many cases of postdiphtheritic paralysis presenting all the symptoms mentioned by Dr. Fallis. In some of our cases deglutition was impossible for a period of from one week to sixteen days. To sustain life through this period it was necessary to feed the patients by means of an œsophageal tube. After the tube was dispensed with swallowing continued difficult for some time. The vast majority of our patients recovered. Of 13 cases observed by Cadet de Gassicourt, 6 died.

Lastly, *tendon reflex paralysis* is very common. Indeed, it is said

to be the most frequent of all the paralyses, probably occurring in one-third to one-half of all well-marked cases of diphtheria. Hughlings Jackson called attention to the fact that loss of knee-jerk is usually one of the earliest symptoms of paralysis. Dr. R. L. McDonnell, of Canada, believes it is present in many cases of diphtheria from the very first day of the illness. It is not only the earliest of the paralytic symptoms to appear, but is also of longest duration. In many cases normal reflex only returns after an interval of four to six months.

The frequency of postdiphtheritic paralysis varies in different seasons, and, as already stated, in different epidemics. It has been found to occur in from 10 to 30 per cent. of all cases of diphtheria. The affection is never permanent. Its duration is from two to six months, counting from the time it first appears until normal motion is restored in all muscles.

Pseudodiphtheria.—The term pseudo- or false diphtheria is now commonly applied to an inflammatory affection of the throat characterized by the appearance of a peculiar exudation in which the Klebs-Loeffler bacillus is absent. It may occur primarily as a catarrhal inflammation of the fauces, in which case it is rarely severe, except when the larynx is involved; or it may occur secondarily in the course of some other affection, like scarlet fever or measles, when it is frequently fatal.

While pseudodiphtheria is often seen associated with scarlet fever or measles, yet it must be remembered that true diphtheria not infrequently coexists with either of these diseases. Most writers believe that when pseudodiphtheria occurs in the course of scarlet fever or measles it is more liable to appear at the height of the primary disease, while true diphtheria more often develops during convalescence. Our experience leads us to believe that this is true with reference to measles only.

It is now well known that pseudodiphtheria is usually due to the streptococcus pyogenes. This organism may be found alone in the exudation, but commonly the staphylococcus aureus or albus is also present. It is said that the staphylococcus is occasionally the only organism found. The condition of the throat of persons suffering from scarlet fever, measles, and perhaps some other infectious diseases is favorable for the propagation of these germs. They are, indeed, often found when no exudation is present.

Pseudodiphtheria sometimes occurs as the result of bad hygienic surroundings, such as imperfect drainage, the inhalation of sewer gas, living in damp houses, and the like. Such environments tend to render individuals more susceptible to an inflammatory affection of the throat of a membranous character. The streptococcus organisms are so widely distributed that pseudodiphtheria is liable to occur, not only under bad hygienic surroundings, but in almost any place at any time, provided that the mucous membrane of the throat is found vulnerable to an attack by these organisms. The occurrence of the disease does not depend upon exposure to a previous case, and it rarely prevails epidemically.

In speaking of the communicability of pseudodiphtheria, Holt refers to some important investigations made upon this point by the New York Health Department.¹ He says: "As the result of observations upon 450 cases which were followed, the conclusion was reached that the disease was so slightly contagious (if at all), and usually so mild, that strict isolation and subsequent disinfection were unnecessary. Of 113 cases occurring in 100 families, in only 14 was there a history of exposure to a similar case, and in only 9 was there another case in the same family. In many of the latter a common origin appeared more probable than that one case was derived from another.

"At the present time the general opinion of the profession seems to be that these cases are to a slight degree communicable, to be compared in this respect to ordinary catarrhal colds or possibly to pneumonia. They are probably more contagious in the presence of the poison of scarlet fever or measles."

For the purpose of testing the communicability of pseudodiphtheria, Park² made some very interesting experiments by inoculating human throats with streptococci. He describes the experiments as follows: "A very thick culture was made on agar plates from a severe follicular tonsillitis in a young child, so that there was obtained a luxuriant growth of streptococci growing both in long and short chains, and also of other micrococci. A large amount of these mingled bacteria were, with the permission of the patient, plastered on a swab and then rubbed gently on the right tonsil and into its crypts. He felt a peculiar sensation in the tonsil for some twelve hours; this then passed away, and was probably simply the result of the mechanical irritation.

"The next morning the tonsil appeared healthy except for a small patch in a crypt; from this, and from the throat, cultures were made. The plates gave very numerous colonies of streptococci, while cultures made from the same regions the day previous to the experiment gave very few streptococci.

"A second trial was made in a similar way from a culture of streptococcus pyogenes, eighteen hours old, from a case of extensive pseudomembrane and tonsillar abscess. The results were also entirely negative, except for the increase of streptococci in the throat for some days. With the same streptococcus the tonsils of two other adults were daubed, and with similar negative results.

"These trials having shown that in three throats the application of streptococci from cultures made from virulent cases of tonsillitis produced no effect, a different experiment was tried. On two separate occasions a sterile swab was rubbed on the tonsils in a case of severe tonsillitis, and then immediately rubbed on a healthy tonsil. In neither case was there any inflammation excited. On the third day after the last experiment a sudden fall in the temperature occurred, and after exposure a follicular tonsillitis developed, such as frequently has followed previous similar exposures."

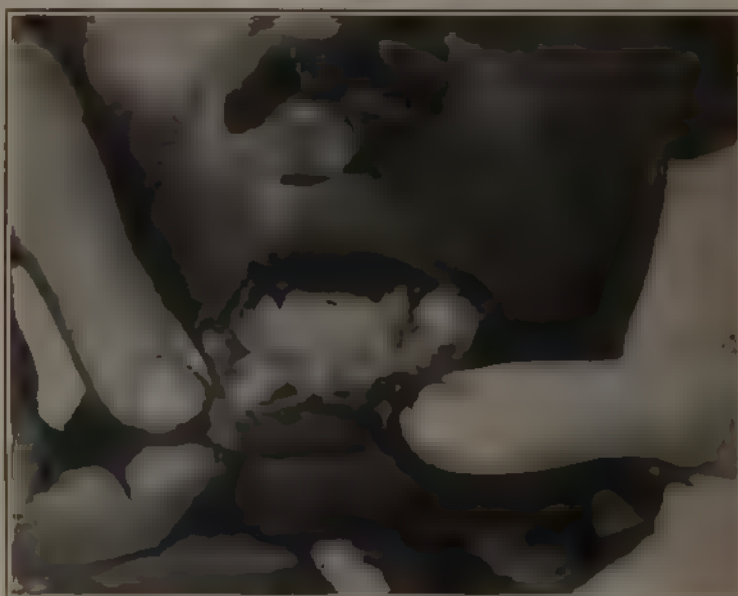
¹ Diseases of Infancy and Childhood.

² Loomis-Thompson, American System of Practical Medicine.

These experiments seem to warrant the conclusion, as Park says, "that the pyogenic cocci are not sufficient, as a rule, to excite an inflammation in the throat." Or, in other words, that the presence of streptococci in the throat are probably harmless so long as the mucous membrane is normal or intact.

In primary cases the disease makes its appearance like an ordinary sore throat. There may be vomiting, slight rigors, headache, general pains, painful deglutition, and fever. The constitutional symptoms are usually well marked at the beginning. During the second or third day of the disease the temperature may rise to 103° to 104° F., but it quickly falls and the other symptoms also subside. On inspecting the

FIG. 9*



A case of pseudodiphtheria in which the exudate covered portions of the upper lip, buccal mucous membrane, and fauces. Diphtheria bacilli were absent, but streptococci and staphylococci were present.

throat the mucous membrane is found reddened and the tonsils swollen. Very soon an exudation appears upon the tonsils, and sometimes upon other parts of the fauces and the buccal mucous membrane also. The exudate is grayish in color, shreddy or pultaceous, and seems to lie upon the surface, as it may be readily removed with a cotton swab. It does not remain long, usually disappearing in three or four days. The inflammation of the throat is often more marked than in genuine diphtheria, and swelling of the lymphatic glands in the neck may be seen, though this is not excessive in mild cases.

In many cases of pseudodiphtheria in which the disease is secondary to another affection the symptoms are as mild as those just described.

But frequently the local manifestations are as severe as in the worst forms of pharyngeal diphtheria, and the constitutional symptoms as well marked as in the septic form of that disease. Indeed, the clinical description given of scarlatina anginosa by some of the older writers is not essentially different from that of septic diphtheria, at least so far as the greater part of the local and constitutional symptoms are concerned.

In scarlet fever the streptococcic process is liable to set in at an early stage of the disease. In severe cases the process may reach its maximum in the latter part of the first week, and continue for two weeks or longer. The disease almost always involves the nose as well as the fauces, and very frequently extends to the middle ear, giving rise to a suppurative otitis media, which may permanently affect the hearing.

The local process in the throat is often more destructive to the tissues than is the case in true diphtheria. Deep sloughing of the tonsils and soft palate is sometimes seen. The lymphatic glands of the neck and the periglandular connective tissue frequently inflame and break down into abscesses. This process also may be attended by considerable loss of tissue, and occasionally is followed by serious hemorrhage.

When pseudodiphtheria occurs secondary to measles the throat involvement is mild as compared with scarlet fever, but the streptococcic process much more frequently extends to the larynx, giving rise to a dangerous form of membranous croup. When this condition develops there is not only danger from stenosis, but also from bronchopneumonia. Sometimes the larynx is involved when there is no sign of exudate in the fauces. Holt believes that this is very infrequent unless the disease is true diphtheria; but we have seen a number of such cases in which the Klebs-Loeffler bacillus was absent.

In secondary cases the temperature, as a rule, ranges higher than in the primary. The pulse rate is more rapid and feeble, and the constitutional symptoms as a whole are severe. When the primary disease is scarlet fever, there is usually restlessness, delirium, great prostration, and albuminuria. Death is liable to result from septic poisoning. If, however, the patient withstands the toxic effects of the streptococcus organisms, the throat symptoms improve, the constitutional disturbance subsides, and recovery takes place as from true diphtheria. But none of the secondary affections peculiar to the latter disease, such as heart-failure and multiple paralysis, are liable to follow.

From a clinical point of view it is often difficult to distinguish between pseudo- and true diphtheria. We believe that in the majority of cases the experienced physician will make a correct diagnosis at the bedside, yet frequently one most skilled in the art of diagnosis will find it impossible to say, in a given case, that the pseudomembranous affection of the throat is not true diphtheria. In such cases, the assistance afforded by bacteriology is of great importance. Holt very truly remarks: "The bacteriologists have taught us to be cautious in pronouncing too positively upon even the mild cases, as it has been clearly shown that some of them may be caused by the most virulent of diphtheria bacilli."

Even in the secondary cases one should not be too ready to exclude true diphtheria in making the diagnosis, for it is well known, as has been already pointed out, that this disease often co-exists with scarlet fever, and not infrequently follows in the wake of measles, particularly when it is prevailing in the neighborhood. The clinical features distinguishing pseudo- from true diphtheria will be considered later.

Except in rare instances of laryngeal involvement, primary pseudo-diphtheria is not a serious malady. Some mortality, however, seems to attend the disease, as death rates varying from nil to 5.5 per cent. have been reported by different observers. According to Holt, of 117 primary cases observed by Park in the Willard Parker Hospital, New York, "the mortality was 3.5 per cent.," while "of 127 cases of true diphtheria seen in the same institution at the same time, the mortality was 34.5 per cent." Out of 34 primary cases of pseudodiphtheria, which, in a limited time, came under the observation of Baginsky (in hospital), the mortality was 5.5 per cent., against 38.2 per cent. from true diphtheria. Holt says: "From the same hospital, Philip has published a report upon 376 cases; 332 of these were true diphtheria, with a mortality of 37 per cent.; 31 were cases of primary pseudo-diphtheria, with no mortality." He also calls attention to the fact that "*The Bulletin of the New York Health Department* contains a report upon 324 cases of pseudodiphtheria in children, with a mortality of 9, or 2.8 per cent.; 4 of the fatal cases complicated scarlet fever; of the primary cases, the mortality was but 1.5 per cent." He adds, "These were not hospital cases."

During the past ten years we have observed in the Municipal Hospital, Philadelphia, 172 cases of pseudodiphtheria, with no deaths. All of these cases were sent in as true diphtheria. There was present on the tonsils, rarely on other parts, a rather loose, filmy exudate, which disappeared in two or three days after admission. Streptococci and other pyogenic organisms were present, but the Klebs-Loeffler bacillus was absent. We have not included in this number the cases of acute follicular tonsillitis which were also sent to the hospital with the mistaken diagnosis of diphtheria.

The mortality among the secondary cases of pseudodiphtheria is often very high. It is highest when the disease occurs secondary to scarlet fever or measles. Holt is inclined to believe that under such conditions it is from 20 to 40 per cent., and that in institutions for young children it not infrequently reaches 70 or 80 per cent., especially when these diseases prevail epidemically. He says that under the latter conditions "the cases complicating measles give, as a rule, a higher mortality than those complicating scarlet fever." This statement accords with our own experience.

As pseudodiphtheria is rarely communicated from one person to another the enforcement of stringent preventive measures, such as quarantine and disinfection, does not seem to be necessary. It is, however, advisable to exclude healthy children from the sick-chamber. In regard to the secondary cases, especially when the primary disease

was scarlet fever or measles, the complicated cases should certainly be separated from the others.

The vast majority of primary cases require but little treatment. The patient should be put to bed and given a light diet. If the bowels are not regular a mild cathartic may be administered. Gargles are of service when the patient is old enough to use them properly. They may consist of almost any mild antiseptic solution. Boric acid in the proportion of 5 to 10 grains to an ounce of water makes a useful gargle; so also does potassium chlorate in solution (teaspoonful to a glass of water). Instead of using gargles, the throat may be sprayed by means of an atomizer with the boric acid solution, or with hydrogen dioxide in the proportion of 1 part to 2 or 3 parts of water. Internally, tinctura ferri chloridi in suitable doses will be found serviceable.

In the secondary cases closer watching is required, as regards both the local and constitutional symptoms. If the child is old enough, more active antiseptic gargles should be used, such as Dobell's solution, perhaps slightly diluted, or 1:5000 or 1:10,000 solution of bichloride of mercury, or hydrogen dioxide, diluted as mentioned above. The gargle should be used every hour or two during the day, but not quite so often through the night.

For accomplishing the purposes of a gargle, the atomizer will often be found more convenient and satisfactory. Dobell's solution, a 1 or 2 per cent. solution of boric acid, or the hydrogen dioxide, will frequently give good results.

If the nares be involved in the streptococcus process, as they frequently are, the cavities should be kept clean by frequent syringing with a bland solution, such as the boric acid, or a warm normal salt solution. The latter has proved very serviceable in our hands. Frequently cleansing the nose of the mucopurulent discharge will go very far toward preventing middle-ear disease, and even septic poisoning.

Drugs administered internally do not influence the course of the disease to any marked degree. We should, however, try to control special symptoms as they arise. If restless, the child should be quieted with morphine, paregoric, or chloral hydrate guarded with a stimulant. Such drugs as the tincture of the chloride of iron, chlorate of potash, quinine, and strychnine, are believed by many practitioners to be of service. Strychnine or digitalis is indicated when the pulse is weak and the arterial tension low. Above all, there is nothing of greater importance in the general management of these cases than stimulation and proper feeding.

When pseudodiphtheria extends to the larynx, especially in early childhood, intubation will probably be required. Inhalation of steam generated under a croup tent will also prove of great service, especially when the primary disease is measles.

THE PATHOLOGY OF DIPHTHERIA.

The most characteristic clinical manifestation of diphtheria is the presence of a pseudomembrane. This membrane may be located in various places along the respiratory and upper digestive tract. Lennox Browne,¹ in a clinical study of 1000 cases, found the membrane above the larynx in 841, or 84.1 per cent., of the cases. The fauces and tonsils were attacked in 672 cases and the fauces and nose in 165. The larynx, alone or with the fauces and nose, was affected in 159, or 15.9 per cent., of the cases.

Holt² found the membrane above the larynx in 63 cases, involving the larynx and structures below in 10 cases, and above and below the larynx in 36 cases.

In a careful study of 220 fatal cases of diphtheria, Councilman, Mallory, and Pearce found membrane at autopsy in 127 cases. It was distributed as follows:

Tonsils	86 cases.	Tongue	9 cases.
Larynx	75 "	Stomach	5 "
Trachea	66 "	Duodenum	1 case.
Pharynx	51 "	Vagina	2 cases.
Nares	48 "	Vulva	1 case.
Bronchi	42 "	Skin of the ear	1 "
Soft palate and uvula	13 "	Conjunctiva	1 "
Esophagus	12 "		

The membrane varies greatly in *appearance*; it may be whitish, grayish, chamois-colored, yellowish, brownish, or almost black. Its density and consistence depend upon the amount of fibrin and other constituents. It is at times granular, friable, and easily broken, and at other times, when the fibrin content is considerable, firm, dense, and elastic. The membrane is more closely adherent to the faucial and laryngeal mucous membrane than to that of the lower respiratory tract, doubtless owing to the difference in the character of the epithelial cells. There is, as a rule, no difficulty in detaching it from the trachea without the production of an abrasion.

Histopathology of the Membrane.—The first important contribution to our knowledge of this subject was made by E. Wagner, who regarded the membrane formation as due chiefly to a peculiar metamorphosis of the epithelial cells. The cells degenerate, fuse, and become converted into a reticular membrane. Cornil and Ranvier confirmed Wagner's observations and declared their belief that the cells contained a mucin-like substance and not fibrin.

Weigert regarded the membrane formation to be the combined result of a coagulation necrosis and a fibrinous exudation, with the necrotic cells and the fibrin both contributing to it.

Peters was of the opinion that the thick, dense diphtheria membrane was formed by a hyaline degeneration of both the epithelial and exudation cells.

¹ Diphtheria and its Associates, London, 1895.

² Loc. cit., p. 257.

Orth differentiates two distinct forms of structure in the membrane: one an exudative membrane consisting of a fibrin meshwork and leukocytes, and the other resulting from a fibrinoid degeneration of leukocytes and epithelial cells; the latter is dense, elastic, and adherent. In addition to the foregoing writers, Oertel, Heubner, Baumgarten, Baginsky, Middeldorpf and Goldman, Neuman, and others have made interesting studies of the diphtheria membrane.

Councilman, Mallory, and Pearce distinguish, microscopically, two distinct varieties of the membrane corresponding to the differences observed macroscopically. The dense, firm, elastic membrane which can be stripped off in large flakes is composed of a reticular structure with beams of uniform size. The reticulum contains masses consisting of leukocytes and epithelial cells which have undergone hyaline degeneration.

The other variety of membrane, which macroscopically is characterized by greater friability, is composed of fibrin. The fibrin forms a reticulum just as does the hyaline material, but varies greatly in the size of the fibres and the spaces. The spaces may contain numerous leukocytes, either well preserved or broken down.

The fibrinous membrane is often continuous over the entire surface of the tonsil and extends into every crypt. The hyaline membrane never extends into the crypts, though occasionally small masses of hyaline reticulum are found in them.

The changes in the tissues observed by the above investigators are summarized as follows: The first step in the membrane formation is degeneration and necrosis of the epithelium, often preceded by active proliferation of the nuclei of the cells by direct division. The cells may either break up into detritus or become changed into refractive hyaline masses. An inflammatory exudation rich in fibrin factors comes from the tissues below, and fibrin is formed when this comes in contact with the necrotic epithelium. The fibrin in part is formed into a reticulum around exudation cells and degenerated epithelium; in part it combines with the hyaline degenerated cells to form a hyaline membrane. The latter is most often formed on those surfaces which are covered with epithelium having several layers of cells. The fibrinous membrane is formed both in the surface and in the tissues. The membrane is never formed primarily on an intact epithelial surface, but it may extend over it. There is nothing specific in the membrane formation in diphtheria, as typical hyaline and fibrinous membranes may be found in ovarian cysts in which bacteria play no part; but it is accompanied by degenerative and exudative changes in the tissue beneath.

The connective tissue and bloodvessels undergo a hyaline fibroid degeneration. Necrosis may extend deeply into the tissues, but there is little tendency to ulceration or abscess formation. The degeneration in the mucous glands, particularly of the glandular epithelium, is so pronounced as to be almost specific. The extent of the necrosis in the primary lesions is greater than is found in the action of any other bacteria.

Diphtheria bacilli were never found growing in the living tissue or in connection with those degenerative changes in the epithelium seen in the beginning. They were found in the necrotic tissue and in the exudation, usually only in the latter. The bacillus shows an affinity for solid structures and is found rather on the reticulum than in the spaces between. The beginning of the lesions is probably due to the toxic action of the bacilli possibly growing in the fluids of the mouth or throat. When necrosis is once produced the necrotic tissue forms a suitable culture medium. The membrane and necrotic tissue are often invaded by pyogenic cocci and by fungi.

Heart.—The pronounced clinical evidence of involvement of the cardiac muscle has led to extensive investigations of the underlying pathological changes in the heart. This subject has received careful study on the part of many pathologists.

Hayem was the first to call attention to the granular and fatty degeneration of the heart muscle and to changes in the vessels and interstitial tissue. Rosenbach noted a granular and waxy degeneration of the muscles and a cell exudation into the interstitial tissue.

In 2 cases of suddenly fatal diphtheria Birch-Hirschfeld found evidences of acute interstitial myocarditis. Martin regards the myocardial change to be secondary and a result of acute endarteritis of the coronary arteries.

One of the most important studies of the heart in diphtheria has been contributed by Romberg,¹ who made careful examinations in 8 cases. He found that the cardiac muscle was not uniformly affected, but that some portions might be normal and other areas show extensive changes.

Small foci of leukocytic infiltration were found around the smaller coronary arteries, but the most important lesion was the degeneration of the cardiac muscle. The degenerated fibres had a peculiar vacuolation in the centre and were without nuclei. The nuclei undergo hypertrophy with an accompanying vesicular condition. The inner and outer portions of the myocardium showed most degeneration.

Focal interstitial changes, most common beneath the pericardium, were present in all cases. In 5 of Romberg's cases pericarditis was present, and in 3 there was endocarditis.

Hesse² made a study of the heart in 29 cases of diphtheria. The parenchymatous changes were not marked under three days, and were more pronounced on the left side. In 25 out of 29 cases interstitial myocarditis was present, and in 4 it was marked. It was noticeable in the first week, but was more pronounced later. The interstitial changes were more frequent in the left ventricle. The leukocytic infiltration was believed to be due to an increased penetrability of the vessel walls which were acted on by the toxin.

Papkow, who examined a number of hearts of patients who died on the third or fourth day, found extensive fragmentation of the muscle

¹ Ueber die Erkrankung des Herz muskels bei typhus abdom. Scharlach und Diphtherie, Deutsche Archiv f. klin. Med., 1891, Bd. xlviii.

² Beiträge zur path. Anatomie des Diphtherie Herzens, Jahrbuch f. Kinderheilk., 1893, Bd. xxxvi.

fibres, with white and red cells between the fragments. The fragmentation was caused by the swelling and destruction of the cement substances. This is an early change, while the waxy degeneration and interstitial infiltration occur later.

Welch and Flexner found fatty degeneration and necrosis of the muscle fibres. Flexner later described swelling and deeper staining of the nuclei, with final disappearance.

Councilman, Mallory, and Pearce have made an extended series of careful examinations of the cardiac muscle in 60 cases of diphtheria. The results of this valuable study are herewith presented: Fatty degeneration of the muscular fibres, varying in extent, was found in 36 of the 60 cases; there were probably more than this number, as only 40 hearts were examined in the fresh state, and of this number 29 showed fatty change.

This degeneration varies in extent, at times affecting the myocardium generally, and at times in foci. The fatty change accompanies and appears to precede more advanced forms of degeneration which lead to complete destruction of the muscle.

The sarcous elements become swollen, broken, and converted into hyaline masses. Vacuolation, fragmentation, and fracture of the degenerated fibres are often seen. Simple fatty degeneration is found in severe cases of short duration, and the more extensive degenerations in protracted cases. The degenerations are due to the bacterial toxin, and account for the impairment of the heart function.

Two kinds of interstitial lesions are found. In the one there are focal collections of plasma and lymphoid cells, which may be accompanied by an independent myocardial degeneration, analogous to acute interstitial nephritis. In the other the interstitial change is secondary to the muscle degeneration. This form may lead to excessive connective-tissue formation and a fibrous myocarditis.

Thrombosis is not infrequently seen as a result of primary necrosis of the endocardium. The only bloodvessel change of interest is proliferation of the intima, which is also observed in other organs.

Lungs.—Pulmonary complications are present in a very large proportion of fatal cases of diphtheria and commonly determine the lethal outcome.

The lesion found is a bronchopneumonia of varying extent. Holt¹ says that in infants and young children bronchopneumonia is found at autopsy in at least three-quarters of the cases. Councilman, Mallory, and Pearce found bronchopneumonia in 131 out of 220 post-mortem examinations; 98 of these were in cases of diphtheria only, and 33 were in diphtheria complicated with scarlet fever or measles. The lung complication was much more frequently observed in patients in whom the larynx, trachea, and the bronchi were the seat of membrane. It is believed that the most important factor in the production of these pneumonias is the aspiration into the lungs of micro-organisms, chiefly micrococci.

¹ Loc. cit.

Of the 131 cases of bronchopneumonia, the areas were discrete in 76 and confluent in 55. In the majority of cases the posterior portion of the lung was affected, and especially the lower lobes. The bronchi were affected in the majority of cases. The mucous membrane of the large tubes was reddened and covered with exudation; drops of pus could usually be forced from the small bronchi by pressing the cut surface of the lung.

In 43 cases there was a fibrinous exudation in the bronchi, forming in the larger ones a distinct membrane and completely filling the smaller.

Councilman, Mallory, and Pearce conclude that there is no organ in which lesions accompanying diphtheritic infection are so generally found or so serious as in the lung. In very many cases they are so extensive that death may be considered as due rather to the condition of the lungs than to the throat affection. The essential lesion is bronchopneumonia; true acute lobar pneumonia was never found. The cases resembling lobar pneumonia were found on close examination to be cases of extensive confluent bronchopneumonia. The character of the exudation varies; it may be fibrinous, hemorrhagic, serous, or almost entirely cellular; rarely it may be hyaline. Atelectasis is commonly present in varying extent, and the same is true of emphysema.

The cellular exudate is in part made up of leukocytes and in part derived from proliferation of the lining of the membrane. Lymphoid and plasma cells are also found. In some cases there is organization of the exudation and connective-tissue formation within the air spaces. The lining epithelium of the air vesicles shows proliferation. Necrosis, in some cases leading to abscess, is not an uncommon feature.

Large objects considered to be marrow cells which in many cases have undergone degeneration are frequently found in the capillaries; it is possible that these have been frequently mistaken for hyaline thrombi. Thrombi are occasionally found in the large vessels, but not in the capillaries. The lymphatics are commonly dilated and contain coagulated albumin, fibrin, or cells. They are often found packed with lymphoid and plasma cells, and large cells similar to those seen in the air spaces. (This summary is based upon a microscopic study of the lungs in 133 cases.)

Bacteriology of Complicating Bronchopneumonia.—Considerable difference of opinion has existed as to the comparative influence of the diphtheria bacilli and other organisms in the causation of pneumonia complicating diphtheria.

Thaon, in 1885, was the first to study the relation of the diphtheria organism to secondary bronchopneumonia. He showed microscopically in the lung tissues the relation of the bacilli to the inflammatory process. The diphtheria bacillus was not found alone, but in association with various cocci.

Loeffler, in his study of the bacteriology of diphtheria in 1884, reported the presence of the diphtheria bacillus in the lung, but regarded it as a post-mortem invasion.

Various observers since this time have published the results of their study of this subject. These reports exhibit extremely divergent findings. For instance, Wright and Stokes in 1895 found the diphtheria bacillus in the lungs in 18 out of 19 cases, in 8 of which it occurred in pure culture. On the other hand, Sims Woodhead, in the same year, found the diphtheria organism in but 5 cases in 50 autopsies. Northrup and Prudden in 1889 found the diphtheria bacillus absent in the lungs of every one of 17 cases examined; streptococci were present in all, and staphylococci in 13 cases.

In a series of 88 cases of diphtheria in which cultures were made from the lungs by Councilman, Mallory, and Pearce, the diphtheria bacillus was found in 49 cases, in 15 of which it appeared in pure culture. The streptococcus was present in 51 cases, in 15 of which it was found alone. The staphylococcus aureus was noted in 27 cases, and the pneumococcus in 10.

These writers conclude that, "contrary to the results obtained from cultures, the pneumococcus must be considered the principal agent in producing the lung affection. The diphtheria bacilli are frequently found and may be the cause of bronchitis with membrane formation, of purulent exudation, of bronchopneumonia, necrosis, and abscess. They are often found in the lung in much greater numbers than in any other situation, and there may be but little change in the tissue around them."

It should be stated that Councilman, Mallory, and Pearce found the pneumococcus 59 times in microscopic sections and 11 times in cultures made from the same cases. Diphtheria bacilli were found 60 times in cultures and 38 times in sections; streptococci 53 times in cultures and 29 times in sections.

Flexner inoculated the trachea of rabbits with diphtheria bacilli and induced pneumonia in a short time. He believed the infection to be produced directly and also through the blood and lymph channels.

Pleural Membranes.—Councilman, Mallory, and Pearce stated that in 18 cases there was pleurisy with fibrinous exudation, 1 with sero-fibrinous exudation, in 7 empyema, in 1 pyopneumothorax, and in 1 hemorrhage into the pleural cavity. Small pleural ecchymoses, irregular in shape, were found frequently, chiefly over the surface of the lower and posterior lobes.

Spleen.—The changes in the spleen in diphtheria have been studied by Bizzozero, Oertel, Müller, Katzenstein, Ziegler, Ribbert, Waschke-witch, Babes, Flexner, and Councilman, Mallory, and Pearce, by whom the above writers are mentioned. Most of these observers describe, as the salient features of the alterations in the spleen, the presence of large, phagocytic, epithelioid cells in the lymph nodules and a necrosis of the lymphoid cells.

Flexner found the lesions in the splenic lymph nodules similar to those in lymph nodes, save that in the former the nuclear fragments were not so often seen in phagocytic cells. The pulp exhibited hyperplasia of the reticular and vascular endothelia, with nuclear destruction of the

cells, both within and without the vessels. Waschewitch examined the spleen of diphtheria and other patients in a large number of cases. Large epithelioid cells were observed in 21 out of 24 cases of diphtheria, and in 11 out of 170 other spleens examined. He believes that these cells are not characteristic of diphtheria, but may be found quite often in children dying of other diseases.

Councilman, Mallory, and Pearce state that there is but little change in the gross appearance of the spleen; it is generally firm, not distended, with smooth capsule. As a rule the lymph nodules are distinctly visible on section, and at times very prominent. The size of the organ varies, but usually within normal limits. The spleen was examined microscopically in 181 cases, from the second to the one hundred and eighth day of the disease, and in subjects from ten months to sixty years of age. Most of the specimens examined were from patients under four years of age and under ten days' duration of the disease. The most conspicuous change in the lymph nodules was the formation of small areas composed of epithelioid cells of hyaline material and of a variable amount of nuclear detritus. This varied according to the duration of the disease.

The epithelioid formation usually occurred early and the hyaline change late. Such areas were found in 91 of 181 cases examined. The epithelioid cells were large, with variously shaped vesicular nuclei, and finely granular protoplasm; they resembled the epithelioid cells found in tubercle. They were formed in the same way as those seen in the lymph nodes. The epithelioid cells are phagocytic and contain a nuclear detritus which is derived from the contained lymphoid cells.

In 17 of the 181 cases there was well-marked degeneration of the arteries in the lymph nodules. The process was limited to the arteries in the lymph nodules. There was hyaline degeneration of the entire vessel wall in many cases, with the hyaline extending from the vessel into the tissue. The lumen of the vessel was narrowed and in some cases almost obliterated. This condition was most pronounced in the acute cases.

Changes in the veins similar to those described by Pearce in scarlet fever were found in 12 cases. These consisted chiefly of an accumulation of lymphoid and plasma cells beneath the epithelium of the intima.

Plasma cells were found in the spleen in large number in the later stages; this suggests that this organ may play an important role in their formation. No bacteria were found in the sections.

Alimentary Canal.—In 1888 Smirnow published a report of 6 cases of pharyngeal diphtheria in which distinct membrane was found in the stomach. The membrane resulted from an inflammatory, fibrinous exudation in 3 cases, and in the other 3 it was due to a hyaline degeneration of the granular and surface epithelium.

Cronmeyer, in an analysis of 459 cases of diphtheria, mentions 29 cases of diphtheria of the stomach.

Councilman, Mallory, and Pearce found 5 cases among 220 autopsies in which a definite diphtheritic membrane was present in the stomach.

In one case almost the entire surface of the gastric mucosa was covered with a thick, ragged, grayish-brown membrane, which, on removal, left a red, granular surface beneath. In the other cases the formation of the membrane was not extensive, and was limited to lines on the surface of the rugæ. Various bacteria were found in the membrane, but there were very few diphtheria bacilli. Upon culture, however, abundant bacilli were found in these cases.

The *intestinal mucous membrane* showed but few gross changes. It varied considerably in thickness, in some cases being decidedly atrophic. The most marked change was the hyperplasia of the lymphoid structures. Peyer's patches were in some cases so swollen as to resemble those seen in the early stage of typhoid fever. The swelling was rarely homogeneous, but the single lymph nodules or groups of them could be distinguished, forming round or elongated elevations with pits or furrows between them. The solitary lymph glands in both large and small intestines stood out prominently. Microscopic examinations were made in 60 cases. The changes in the intestinal lymph nodules were identical with but less pronounced than those in the lymph nodes generally. There was marked hyperplasia, and in 20 cases focal lesions, such as are seen in the spleen and lymph nodes. The vascular endothelium was swollen and proliferated, and often contained lymphoid cells.

Bizzozero and Oertel found similar alterations to those here described.

Welch and Flexner, in experimental diphtheria, found in addition to necrosis in the lymph nodules a general diffuse necrosis affecting the glandular epithelium.

Courmont, Dogan and Paviot injected dogs with diphtheria toxin and produced hyperæmia and degeneration of Peyer's patches.

The changes above described are probably due to the action of toxins, absorbed not from the alimentary canal, but from the blood current.

Liver.—Oertel was one of the first observers to study the microscopic changes in the liver in diphtheria. He found small hemorrhages beneath the peritoneum and in the more superficial parts of the liver substance. He also noted a leukocytic infiltration of the subperitoneal and periportal connective tissue, with a fatty degeneration of the liver cells in the neighborhood of the cell invasion.

Katzenstein observed cloudy swelling and fatty degeneration of the liver cells, exudation of leukocytes in the periportal connective tissue, nuclear degeneration, and in a few cases hyaline degeneration of the walls of the capillaries.

Gaston, in a study of the hepatic changes in various infectious processes, described in diphtheria congestion of the vessels, fatty degeneration of liver cells, particularly in the centre of the lobules, and embryonic cell infiltration of the periportal spaces.

Barbacci found abundant leukocytes in the hepatic vessels, swelling of the capillary epithelium, and hyaline degeneration of the walls. The liver cells were granular, swollen and oedematous, and showed various

degenerative changes. The leukocytic infiltration of the periportal connective tissue was almost constant.

Babes found, in diphtheria produced experimentally in animals, the liver cells swollen, pale, granular, and, in places, filled with fat. In addition there were areas of leukocytic infiltration and swelling of the endothelial lining of the bloodvessels.

Welch and Flexner have thoroughly studied the hepatic changes in experimentally induced diphtheria. The most important changes were necrosis of liver cells, affecting chiefly definite groups of cells, leukocytic infiltration in the necrotic foci, and swelling and proliferation of the endothelial cells of the capillaries.

Baldassari found cloudy swelling, fatty degeneration and necrosis of liver cells, and fragmentation of the chromatin network of the nuclei.

Councilman, Mallory, and Pearce examined the liver in 180 cases of diphtheria. There were no characteristic gross appearances. It was generally slightly swollen and somewhat tense and congested. In some cases the congestion was pronounced, but in others the liver was pale and cloudy, due largely to fatty degeneration.

Microscopically, the most constant lesion was swelling of the cells with increased granulation; this was most marked in the centre of the lobules.

In place of the fine, even granulation of the normal cell, coarse granules of irregular size appear.

It was difficult to judge of the presence and degree of fatty degeneration. Many of the liver cells contained fat-vacuoles. The most extensive fatty degeneration consisted of an actual necrosis of the liver cells. The necrosis was most marked about the hepatic veins and was always found affecting groups of cells. In most cases the necrosis is confined to the centres of scattered lobules; in others almost all the lobules in the section are affected. The disseminated foci were not so common as the central necrosis; they were found in but 7 of the 180 cases, whereas the central necroses were found in 22. The two processes were but rarely associated.

Flexner regards the necrosis in experimental diphtheria as due to injury of the vessel wall at some point, allowing transudation to take place more freely. He believes the injury is produced at some period of greater concentration of the toxin and at a point where the circulation is slowed or at a standstill.

In addition to the changes above mentioned there is occasionally seen a slight hyaline degeneration of the capillary walls; the capillaries constantly contain an increased number of cells which are derived in part from proliferation of the endothelium, and in part from cell infiltration.

The lesions in the liver in diphtheria are not characteristic of the disease; similar changes are found in other infectious processes. No diphtheria bacilli were found in the microscopic sections. The hepatic lesions in human diphtheria differ from those experimentally induced in animals, chiefly in the greater frequency of the central situation of the necroses.

Kidneys.—The pathological changes in the kidneys in diphtheria have been studied by Brault, Fürbringer, Fischl, Oertel, Bernard and Felsenthal, Reiche, Katzenstein, and others. The alterations induced by experimental diphtheria have been specially described by Flexner.

Councilman, Mallory, and Pearce examined the kidneys microscopically in 171 cases. The ages of the patients varied from two months to thirty years, and averaged three and three-quarter years. It was found possible to divide the kidneys into five classes according to the microscopic findings: 1. Those in which degeneration of the epithelium was the chief or the only lesion. 2. Those in which acute interstitial changes consisting of cell accumulations in the vessels and interstitial tissue were present. 3. Those in which the chief lesions were found in the glomeruli. 4. Those in which hemorrhages into the tubules were present. 5. Those in which chronic interstitial lesions were present as shown by atrophied glomeruli and increase in the connective tissue.

1. Degenerative Changes.—Degenerative changes of varying grades were found in 112 of the 171 cases examined. Many kidneys, almost or quite normal in appearance, showed under the microscope a considerable degree of degeneration. The degeneration was slight in 26 cases, moderate in 38, marked in 37, and extreme in 9 cases. The most extreme degree was found in severe cases dying shortly after entry into the hospital.

Fatty degeneration, as determined by examination of frozen sections, was only slight in degree; it occurred in 44 out of 58 cases examined in this manner.

Some degree of hyaline degeneration was found in almost all the cases, affecting prominently the proximal convoluted tubules. Casts were present in practically all of the cases, especially when the hyaline degeneration was pronounced.

The most constant change seen in the glomeruli consisted of a small amount of granular coagulum between the tuft and the wall.

In 40 cases of simple degeneration the urinary record is available. Albumin was found in 33 of the cases. There was, with some exceptions, a general agreement between the presence of albumin and the degree of degeneration.

There appeared to be no relation between the character of the degeneration and general infection with various bacteria. In the 110 cases a general infection with diphtheria bacilli was noted in 20 cases, with the streptococcus in 29 cases, with the staphylococcus aureus in 4 cases, and with the pneumococcus in 3 cases. In the 9 cases of severe degeneration general infection was noted but once, and that with the streptococcus.

2. Acute Interstitial Changes.—Acute interstitial nephritis, evidenced by infiltration of the interstitial tissue with cells of the plasma type, was present in 43 of the cases. The kidneys were but slightly, if at all, enlarged, save in the most marked cases, when considerable swelling was present. The interstitial infiltration was general in all parts of the kidney, but was more intense in foci; most of the cells were plasma

cells with typical nucleus and protoplasm. Lymphoid cells and, in severe cases, large phagocytic cells were also present. The amount of epithelial degeneration varied in different cases.

The infiltrating cells were usually limited to the interstitial tissue; the changes were accompanied by alterations in the vessels, the cell infiltration at times almost obscuring them. The degeneration found in foci of intense infiltration appears to depend on malnutrition resulting from blocking of the vessels by the cells.

In all of the interstitial cases the duration of the disease was more prolonged than in the cases of simple degeneration. The average duration of the illness was twenty-one and one-half days. The interstitial process apparently takes some time for its development, and the cases dying early do not, as a rule, show the process at its maximum. Mixed infections with scarlet fever and measles are more apt to cause interstitial changes than simple degeneration. The urine was tested for albumin in 15 cases, in 14 of which it was found present.

3. Glomerular Changes.—This variety of the disease was found in 11 cases, in all of which the glomerular changes were the predominating ones. Lesions of the glomeruli were uncommon in the cases of simple degeneration and in those showing interstitial involvement.

The first evidence of change in the glomeruli is increase in the number of cells. The endothelial lining of the vessels undergoes proliferation and occludes the vessel. Later a hyaline degeneration of the cells and the vessel walls takes place.

Glomerular nephritis was present in subjects averaging a greater age than the degeneration and interstitial cases. The average duration of the disease at the time of autopsy was also greater.

4. Hemorrhage.—Slight hemorrhages in the kidney were seen in 3 cases, but true hemorrhagic nephritis was noted in but 1. The red blood cells were found chiefly in the tubules and the interstitial tissue. The rarity of hemorrhagic cases was considered surprising.

5. Chronic Cases.—In 4 cases chronic changes were present, as evidenced by atrophy of the tubules and increase in connective tissue. In these cases death occurred at entirely too early a date to attribute the changes to diphtheria; the lesions were evidently due to some antecedent disease.

Councilman, Mallory, and Pearce conclude that lesions of the kidney, varying from simple degeneration to the more serious conditions of acute nephritis, are found in all fatal cases of diphtheria; there is, however, no type of lesion peculiar to the disease.

Lymph Nodes.—The changes in the lymph glands have been studied by Bizzozero, Oertel, Bullock and Schmorl, Barbacci, Bezancon and Labbe, Flexner, and Councilman, Mallory, and Pearce. The most constant changes observed by these investigators have been a marked cellular infiltration and the presence of necrosis. Bullock and Schmorl found diphtheria bacilli in the nodes in 11 out of 14 cases.

Councilman, Mallory, and Pearce examined the lymph nodes in 109 cases. They were constantly the seat of pathological changes.

The nodes most involved are those nearest to the seat of exudate—the tonsils and the cervical glands. The distant nodes are very rarely affected.

The lesions are most pronounced in severe cases, in which a fatal termination occurs early. Two varieties of lesions are described:

1. The ordinary lesions, which may follow an injury of almost any sort and which consist in congestion, hemorrhage, and diffuse and circumscribed necrosis. Numerous new cells are found which are derived partly from the lymphoid cells, and partly from proliferation of the endothelial cells of the sinuses and reticulum. The swelling of the nodes is due chiefly to congestion, hemorrhage, and dilatation of the sinuses; the lymphoid cells do not increase perceptibly in number.

2. Lesions which are distinctive of diphtheria, but which may be found in other infectious diseases in children. Foci are formed which are similar in appearance to miliary tubercles; these are the result of a combination of processes—proliferation, phagocytosis, and degeneration. Large epithelioid cells are formed from proliferation of the endothelial cells of the reticulum and vessels. These devour lymphoid cells, and they themselves ultimately undergo necrosis. Bacteria seem to exert no direct influence in the production of these lesions, and were not found in the nodes.

The lesions are believed to be due to the absorption of the toxic products of the diphtheria bacilli and other organisms.

The lesions found in the tonsils differed somewhat from those seen in other lymphoid structures. They were constantly present, and in most cases more pronounced than in the glands.

Thymus.—Flexner studied the changes in the thymus gland in experimentally induced diphtheria in animals. He called attention to the frequency with which the degenerated cells occurred in the neighborhood of the Hassel bodies. The changes in general were similar to those observed in the lymph nodes.

Councilman, Mallory, and Pearce examined the thymus in 20 cases. The principal change found was degeneration of the lymphoid cells. The degenerated cells were usually seen in large cells with vesicular nuclei; the changes were most marked in the vicinity of the Hassel bodies. There was dilatation of the lymphatics and hyaline degeneration of the walls of the vessels. No bacteria were found in the sections.

Skeletal Muscles.—Councilman, Mallory, and Pearce state that where fatty degenerations of the heart and the nervous system are present, a similar change will be found in the skeletal muscles. In one case in which the nerve fibres of the central nervous system and of the peripheral nerves showed marked fatty degeneration, the muscles of the tongue, of the ulnar side of the forearm, the sartorius muscle, and the biceps of the thigh exhibited a similar degeneration.

In another case where fatty degeneration of the heart and nervous system was pronounced the muscles of the tongue, the diaphragm, and the tibialis anticus were likewise degenerated.

Pancreas, Adrenals, Thyroid Gland, Salivary Glands, Testicles, Pituitary Body.—No gross changes were observed in these glands by Councilman, Mallory, and Pearce; neither did a careful microscopic examination reveal the presence of pathological changes.

In one case the submaxillary gland showed superficial necrosis and purulent infiltration due to extensive inflammation from the throat.

Welch, Flexner, and Wright commonly observed congestion, hemorrhage, and focal necrosis in the adrenal glands in experimental diphtheria, but such changes apparently do not occur in this disease in the human subject.

Nervous System.—Councilman, Mallory, and Pearce refer to a study of certain nerve structures made in 28 of their cases by Thomas and Steensland. The cases were selected either on account of the presence of cardiac symptoms, paralysis, or the severity of the disease. Various cranial and other nerves were submitted to careful microscopic study. In all of them some grade of fatty degeneration was noted. The degeneration seems almost invariably to begin in the myelin sheath. The change in the axis cylinder consists chiefly of an irregular swelling which often causes it to present a beaded appearance.

The cerebrum was examined five times, the cerebellum twice, the pons three times, the medulla four times, and the cord seven times. In all of these examinations a varying degree of fatty degeneration was present in the white substance. The same change was noted in the anterior and posterior nerve roots.

In general it may be said that a slight to a marked diffuse fatty degeneration, involving the central nerve fibres and their peripheral extensions, occurs in certain cases of diphtheria.

Bone-marrow.—Councilman, Mallory, and Pearce examined the bone-marrow in 48 cases of diphtheria. Of this number all but 3 were children. In all of the cases the marrow was hyperplastic, although in the 3 adults the hyperplasia was less pronounced. In the latter the marrow was reddish with areas of yellow fat.

In the children the marrow varied in appearance, but was usually red, of firm consistency, and removable in solid pieces.

Very little connective tissue was found in the marrow, and that was along the arteries. The veins were numerous and the walls like those of capillaries; it is through these thin walls that the marrow cells appear to enter the blood.

The changes in the marrow in diphtheria are not distinctive of the disease, as they are also found in other infectious diseases.

Blood.—According to Baginsky there is an increased coagulability of the blood in diphtheria due to the action of the toxin on the blood stream through weakness of the heart, and also as a result of the lowered blood pressure and changes in the lining of the bloodvessels. This, it is claimed, may lead to the formation of thrombi in the heart or bloodvessels. In severe septic cases a thinning or dissolution of the blood occurs, which may cause hemorrhages in various tissues.

The specific gravity is said by Grawitz to be raised at the height of

the disease, both in diphtheria in man, and in experimental diphtheria in animals.

Red Cells.—During the first few days of the disease the red corpuscles are about normal in number, according to the investigations of Morse, Ewing, Engel, and Billings. From the fifth to the fifteenth days, Billings observed an average loss of 510,000 cells per cubic millimetre. The loss ranged from 470,000 on the third day to 2,040,000 on the sixth. These were in cases not treated by antitoxin. Of 23 severe and carefully counted cases treated with antitoxin, 3 alone exhibited a reduction in the erythrocytes, the loss being less than 400,000 cells per cubic centimetre.

Cabot remarks that “antitoxin largely prevents the anæmia which usually develops in the first five to ten days.” Healthy persons receiving antitoxin, according to a study of 15 cases by Billings, show a moderate loss of red cells in about one-half of the cases; the greatest diminution observed was 930,000 per cubic millimetre.

Hæmoglobin.—A reduction in the hæmoglobin occurs coincidently with the diminution in the number of red cells, but restoration of the former takes place more slowly than the latter. Billings states that in cases treated without antitoxin an average loss of 10 per cent. was noted; whereas, when antitoxin was administered the reduction of the hæmoglobin was less marked.

Leukocytes.—Gabritschewsky, in 1894, was the first to point out the more or less constant hyperleukocytosis in diphtheria. He demonstrated by animal experimentation that the increase in the white cells was due to the action of the diphtheria toxin.

Morse found a leukocytosis in 26 out of 30 cases, Ewing in 49 out of 53, and Billings in 34 out of 36 cases. The grade of the leukocytosis is in a general way proportionate to the severity of the disease. Morse observed very high counts in the fatal septic cases.

Cabot says that when leukocytosis is absent the cases are either very mild or very severe, conditions analogous to those noted in pneumonia and septicæmia. The counts range from normal to 48,000 (Morse), or to 38,000 (Billings). Bouchut counted over 75,000 white cells per cubic millimetre in some of his cases, and Felsenthal found 148,229 in one case.

The white cells ordinarily increase as the disease progresses, and decrease as convalescence sets in.

According to Ewing, the leukocyte count is not influenced by the use of the antitoxin serum, except during the first twenty-four hours after its injection. Within thirty minutes the leukocytes are said to be considerably diminished.

Engel states that antitoxin in the beginning causes a slight increase in the percentage of lymphocytes; in some cases the increase is pronounced. In one case after injection they rose from 24 to 65 per cent.

Engel also emphasizes the bad prognostic import of the presence of a considerable number of myelocytes.

It is generally conceded that an examination of the blood in diph-

theria lends little or no aid in diagnosis. The absence of leukocytosis and the presence of a considerable number of myelocytes would seem to be of ill augury.

THE DIAGNOSIS OF DIPHTHERIA.

As diphtheria is a communicable disease with a decided predilection for young children, among whom it is also most fatal, it is important that an early diagnosis should be made, both with regard to prevention and treatment. Without a history of previous exposure to the infection it is confessedly difficult to recognize the disease in its very earliest manifestations; for there is no throat affection more varied in its clinical aspect and more deceptive in its initial stage than diphtheria. But, fortunately, the disease is not long in revealing its true nature. In the majority of cases the diagnosis is not difficult after the affection has continued for twenty-four hours, since by this time the characteristic exudation may be seen on the tonsils or some part of the fauces. When thus clearly marked the nature of the throat disease is at once apparent on the first examination.

But all cases are not so readily diagnosticated, even by experienced physicians. Neglecting to inspect the throat of a child, who is feverish and indisposed, may sometimes be a reason for failure in making an early diagnosis. While sore throat is one of the earliest symptoms of diphtheria, yet it is a fact that many children, even those old enough to make known their sensations, do not complain of the throat until the disease has made considerable progress.

On his first visit to a child, on account of whose illness he has been summoned, the physician should be careful to examine the fauces, especially when diphtheria is prevailing in the neighborhood. In this way the disease may be discovered early and its spread to other members of the family prevented.

In well-marked cases it is usually not difficult to make the diagnosis. In doubtful cases it may be helpful to know whether the patient has been recently exposed to the infection of diphtheria, scarlet fever, or some other infectious disease. If exposure to diphtheria is known to have occurred, the mildest form of sore throat should be regarded with suspicion and carefully watched for further development. But, in a section of the country where diphtheria is not prevailing, it is probable that a sore throat presenting some of the characteristics of the disease will turn out to be something else.

It sometimes happens that an early diagnosis is not made because the exudation is concealed in the crypts of the tonsils, or in some other depressions of the faucial surface. When thus located it may be brought into view by pushing the tongue depressor far back on the tongue and causing the child to retch slightly; or these surfaces may be exposed to view by having an assistant make firm pressure on the neck near the angle of the jaw while an examination of the throat is being made.

In some cases it is impossible to make a positive diagnosis, clinically,

until the disease has been under observation for two or three days. This is more especially true in some forms of nasal diphtheria, without involvement of the fauces to a greater extent than the occurrence of a general hyperæmia. The uneven surface of the cavities of the nose favors concealment of the disease until it has made some progress. It may then be discovered either by inspecting the nares at their external orifices, or by an examination with a nasal speculum. In nasal diphtheria there is apt to be a mucopurulent discharge from the nose, and when there are seen in this discharge small, white specks, exudate is probably present, although it may not yet be visible. It usually, however, makes its appearance before the disease terminates.

There are no prodromata that are peculiar to diphtheria. The general malaise, followed by headache, nausea and vomiting, so commonly seen, are the forerunners of many other affections also. Even the sore throat, pain in swallowing, tenderness of the glands near the angle of the jaw, and swelling of the neck are all present in the ordinary forms of tonsillitis. The distinguishing feature of diphtheria is the peculiar exudation that appears upon the mucous membrane, particularly in the fauces. A knowledge of the fact that this exudation takes place not only into the epithelium, but also into the subepithelial tissue, is helpful only to a limited extent in solving the problem of diagnosis. Indeed, in many severe cases the diphtheritic process does not penetrate deeply into the mucous membrane, as it peels off quickly and leaves only small areas of superficial ulceration. On the other hand, an exudation of streptococcic origin is sometimes very adherent, and its disappearance may be followed by marked ulceration of the mucous membrane. But in most streptococcic affections of the throat, certainly in the milder varieties, the disease is limited to the tonsils, and the greater part of the exudation may be removed with a cotton swab.

In considering the diagnostic feature of the diphtherial membrane it is necessary to recall some of its characteristics already described. It is deposited not only on the tonsils, but frequently also on the pillars of the fauces, the soft palate, the pharyngeal wall, in the nares, and in the larynx. One of the peculiarities of the membrane is that it is liable to start on some of the small prominences of the fauces, such as the uvula, epiglottis, and the like. As already mentioned, it is also liable to form in some of the small recesses, such as the lacunæ of the tonsils and the ventricles of the larynx. The formation of membrane on the uvula, especially on its posterior surface, is believed by some writers to be almost pathognomonic. When seen on the sides of the uvula it is quite sure to be present on its posterior surface also. Frequently the entire uvula is invested with membrane, which is often shed as a complete cast, resembling, as Trousseau has said, the finger of a glove.

When the diphtherial exudation is examined carefully it is found to be distinctly membranous. It is of a yellowish-white color, and when exfoliated in large pieces or casts and allowed to float in water it bears a strong resemblance to pieces of chamois skin. Lennox Browne's description of the exudation is worth repeating. He says it "begins

almost invariably as a thin, bluish-white deposit, something like a shaving from the boiled white of an egg of the duck, goose, or plover. As the deposit increases in thickness, it gradually becomes more white and opaque, resembling the boiled albumen of a fowl's egg, or it may then partake of a very pale lemon tint. Then it becomes of a yellowish or greenish gray, brown, and sometimes almost black, as the necrotic process advances, or as blood is extravasated. Only in the comparatively uncommon case of a lacunar diphtheria do we see the exudation commencing as discrete spots of deposit, which may be of a yellow color at the very first onset, and, even when coalesced, may never exhibit the pearly or opalescent appearance which characterizes the more ordinary form on its first manifestation." He adds, "The membrane is sometimes plastered, as if put on with a palette knife, or laid on with a trowel." This latter comparison applies with much aptness to what is seen when the entire fauces and soft palate are covered with the exudation.

Adenitis, or more or less enlargement and tenderness of the lymphatic glands of the neck, is a symptom rarely absent. Its importance depends to some extent on the region in which the glands are involved, and the degree of inflammation and swelling. In mild tonsillar diphtheria the cervical glands alone are swollen, but, as a rule, only very slightly. In the more severe cases, including the complex or septic form of the disease, the whole chain of cervical glands is converted into one large mass. The inflammatory enlargement includes also the periglandular cellular tissue. In such cases not only the cervical, but the submaxillary and sometimes the parotid glands are affected.

Catarrhal Croup.—There is frequently some difficulty in distinguishing between membranous croup in its early stage, and catarrhal, spasmodic, or non-specific croup. But if a few of the principal points of difference be borne in mind the difficulty should not be very great. For instance, in membranous croup the symptoms are progressive, being as well marked in the day-time as in the night. The hoarseness gradually increases, so that the child in a short time can speak only in a whisper. The breathing becomes more and more obstructed as the exudation increases; the temperature reaches 100° to 103° F., and the child constantly grows more restless and cyanotic. There is marked recession of the ensiform process of the sternum, and of the lower ribs. These symptoms are not relieved by the relaxing influence of an emetic. Moreover, the characteristic exudation may be present in the fauces. On the other hand, in catarrhal or spasmodic croup the symptoms are usually intermittent, being due to a paroxysmal spasm of the glottis, resulting from subacute laryngitis. In the vast majority of instances the affection occurs at night-time, and more often in the early part of the night. During the day the symptoms, if present at all, are usually much more moderate. The duration of the paroxysm varies from a few minutes to several hours. The voice, though hoarse, is very rarely quite extinct or whispering, and scarcely ever more than temporarily so.

This is a diagnostic point of much value in distinguishing between the two forms of croup. In spasmodic croup an emetic generally gives relief, but does not in membranous croup. The fauces are free from exudate.

Pseudodiphtheria.—We have already remarked that a membranous sore throat, in which the streptococcus is the principal if not the sole organism present, sometimes occurs, and we have pointed out some of the characteristics of this affection in comparison with those of true diphtheria. We repeat that, as a rule, in true diphtheria the exudate is so intimately connected with the mucous membrane that it cannot be removed without injuring the parts, while in pseudodiphtheria it lies upon the surface and may be quite readily removed. It must be admitted, however, that there are many exceptions to this rule. The physician, therefore, will often find it impossible to make a positive diagnosis without a culture and a microscopic examination.

Follicular Tonsillitis.—There is perhaps no throat affection more often mistaken for diphtheria than follicular tonsillitis. It is a very common disease, being more frequently seen in some families than in others. It sometimes spreads as though it were contagious. It begins with sore throat, fever, and tenderness in the neck below the angle of the jaw. There is often a good deal of constitutional disturbance, such as high temperature, headache, and chilliness, with sometimes pain in the back and extremities. The fauces at first are hyperæmic, but the tonsils soon become enlarged and dotted over with rounded masses of whitish material of pinhead size. These dots frequently coalesce, forming quite large patches, particularly in the crypts of the tonsils. The dots or patches consist of a peculiar secretion having incorporated with it epithelial cells. It differs from the diphtherial exudate in that it is readily detached by a swab. The cheesy dots that form on the tonsils will, when crushed between the thumb and finger, emit a fetid odor. The disease is of short duration, and is not followed by sequelæ. The diagnosis is easily made, except in some cases of the mildest form of diphtheria when differentiation may be difficult. In acute quinsy the jaws are stiff, and there is often considerable difficulty in opening the mouth sufficiently wide for a satisfactory inspection of the fauces. Where any doubt is felt as to the nature of the affection it may be readily dispelled by a bacteriological examination.

Herpetic Pharyngitis.—There is usually no great difficulty in recognizing an herpetic pharyngitis, but, like follicular tonsillitis, it is occasionally mistaken for mild diphtheria. If seen in the early stage, before the minute vesicles have disappeared, the diagnosis is easily made; but the ulcers that remain often show a whitish covering, which has often been mistaken for diphtherial exudate. As the ulcers are very small, the whitish concretions are usually seen in the form of dots. It is only when these concretions unite and form a patch that any difficulty is experienced in the diagnosis. It has been said that the presence of an herpetic eruption on some other part of the body would afford presumptive evidence that the throat affection was of the same

nature, but we have often seen herpes labialis in children suffering from diphtheria. Fortunately, in these diseases the clinician does not have to base his diagnosis upon symptoms alone; he can invoke the aid of bacteriology.

Gangrenous Pharyngitis.—In our experience gangrenous pharyngitis is rare in diphtheria. We do not recall having seen a single case. The affection, however, is not uncommon in scarlet fever. The ulcerative action and loss of tissue are much more extensive than that which is seen in diphtheria. The necrotic tissue resulting from the gangrenous process has often been mistaken for diphtherial exudate. The pseudomembrane in this variety of sore throat is, from the beginning, of a dark-gray or brownish color, and is exceedingly offensive. On the other hand, the pseudomembrane of diphtheria is white or yellowish-white in the commencement, and continues so to the end unless it becomes stained with blood. The fœtor in the latter disease is mild in comparison with the former. The diagnosis is not difficult if the case comes under observation at the beginning.

Stomatitis.—In diffuse inflammation of the mucous membrane of the mouth the small ulcers that commonly appear show a whitish covering. This condition not infrequently increases to the extent that many of these ulcers coalesce, forming patches consisting of a whitish, curd-like matter; and the affection often extends gradually to the roof of the mouth, the inside of the cheeks, and may even reach the pharynx. The exudation is usually thin, and sometimes covers evenly a large part of the mucous membrane of the mouth, but more commonly it is seen in irregularly scattered patches and points. When the disease assumes this appearance it is occasionally confounded with diphtheria. In making a diagnosis it is important to note that the exudation is thin and filmy; it never becomes membranous. On parts where it is thicker it is curdy or cheesy.

We have known *gangrenous stomatitis* and even *syphilitic sore throat* to have been mistaken for diphtheria. In view of the general characteristics of these affections the diagnosis is not difficult.

The presence of *albumin* in the urine in diphtheria deserves some notice as a diagnostic sign. We have found it in quite a large proportion of our cases in which the urine was examined. Its presence would be of still greater diagnostic importance were it not true that it is occasionally found in some other varieties of inflammation of the throat.

Since the advent of bacteriology as a science the clinician has at his command a most useful means of determining the diagnosis of diphtheria in all doubtful cases. While every well-informed physician should be familiar with the clinical evidences of the disease, yet as the clinical disguises of this throat affection are so varied it is fortunate that the doubtful points of diagnosis can be solved by bacteriology. Therefore, any consideration of the subject of diagnosis in diphtheria would be regarded as incomplete at the present day without some reference to the means employed to determine the presence of the Klebs-Loeffler bacilli in the pseudomembrane.

The Bacteriological Diagnosis of Diphtheria.

In a patient presenting suspicious clinical evidences of diphtheria, the diagnosis may be firmly established by determining the presence or absence of the diphtheria bacilli in the false membrane. This may be accomplished by examination of (*a*) smears, and (*b*) cultures.

Smears.—In a large percentage of cases a satisfactory result may be obtained from an immediate microscopic examination of the exudate present. A cover-glass is smeared with material taken from the throat by means of a swab. The cover-glass preparation is allowed to dry, is then passed several times through a flame to fix the albumin, and is finally stained with Loeffler's solution of methylene blue. By this means the presence or absence of bacilli may often be determined in a few minutes.

The rapidity with which the examination can be made makes it a procedure of great value, particularly where an immediate diagnosis is a matter of great importance. We have examined a considerable number of smears at the Municipal Hospital, and in these cases we were enabled in the vast majority of cases to predict the subsequent cultural findings.

The procedure just mentioned, however, has only a relative value and should not be depended upon to the exclusion of the culture. The bacilli found in smears are ordinarily much less typical than those grown upon culture media, and the chances of contamination are greater. Abbott¹ says: "There are other organisms present in the mouth cavity, particularly in the mouths of persons having decayed teeth, the morphology of which is so like that of the bacillus of diphtheria that they might easily be mistaken for that organism, if subjected only to the usual method of microscopic examination." He adds, however, that where there is suspicious clinical evidence the direct examination of smears will serve to confirm or negative the diagnosis in the vast majority of cases.

Cultures.—Cultures are ordinarily made with a swab, although a platinum loop may be employed for the purpose. The swab consists of absorbent cotton wrapped around the end of a piece of heavy wire. The swab, enclosed ordinarily in a plugged test-tube, is sterilized by heat.

In taking the culture the tongue should be depressed by means of a spoon or depressor, and the swab firmly rubbed over the surface of the membrane. When no membrane is present, the swab should be brought in contact with the tonsils, faucial pillars, and pharyngeal wall. When laryngeal symptoms alone are present, the swab should be introduced as far down as possible. The moistened cotton is then rubbed lightly over the surface of a tube of Loeffler's blood serum, care being taken to carefully replace the cotton plug. The swab containing the remains of the infected material should be returned to its own tube and subsequently destroyed or disinfected.

¹ The Principles of Bacteriology, 5th ed., 1899, p. 351.

Great care should be taken not to make the culture directly after antiseptic applications have been applied to the throat. It is well in such cases, to wait a half-hour or an hour before culturing. The inoculated tubes are incubated at a temperature of from 99° to 100° F (37° C.) for twelve to fourteen hours, at the end of which time the colonies may be examined.

The gross appearances of the culture are more characteristic at the end of twenty-four hours. The diphtheria bacillus grows so much more rapidly than other mouth organisms upon the surface of Loeffler's blood serum that they are often the only conspicuous colonies present. The colonies are large, round, grayish-white or cream-colored, elevated with irregular periphery, which is less dense in the centre.

Examination of Cultures.—A drop of sterile water is placed upon a clean cover-glass and rubbed up with a couple of colonies which have been detached from the culture media with a platinum loop. The preparation is allowed to dry in the air and is then passed several times through the flame of a Bunsen burner or alcohol lamp. It is then covered with Loeffler's alkaline solution of methylene blue for ten minutes, after which it is rinsed, dried, and mounted in balsam.

The specimen is examined with a one-twelfth-inch oil-immersion lens. Diphtheria bacilli may be found in pure culture, or micrococci of different varieties may also be present.

In order to test the virulence of diphtheria bacilli a guinea-pig is subcutaneously injected with a small quantity of a pure culture in bouillon. Death results in from twenty-four hours to five days, usually within seventy-two hours.

There is intense oedema with congestion and hemorrhage at the site of injection. The changes in the other tissues, according to Abbott, are as follows: Swollen and reddened lymphatic glands, increased serous fluid in the peritoneum, pleura, and pericardium; enlarged and hemorrhagic adrenal bodies; occasionally slightly, swollen spleen; and sometimes fatty degeneration in the liver, kidney, and myocardium. The bacilli are always to be found at the site of inoculation, most abundantly in the grayish-white, fibrinopurulent exudate.

THE PROGNOSIS OF DIPHTHERIA.

The forecast of diphtheria cannot be made with any degree of certainty. The disease itself, to say nothing of the complications that are liable to occur, is so treacherous that it is almost impossible to predict a favorable ending of any attack however mild the earlier symptoms may be. Not infrequently cases that appear to be mild in the beginning and give the best promise of recovery suddenly change into a severe form through extension of the diphtheritic process into the larynx, or the development of some dangerous secondary affection. On the other hand, cases that begin with marked severity, giving rise to gloomy forebodings, often take a favorable change and speedily end in recovery.

So variable are the elements of prognosis in diphtheria that they cannot be considered from any single standpoint. One must take into consideration the prostrating effects of the toxins of the disease; the history, environment, and age of the patient; the complications affecting vital parts during the course of the attack, and the nature of the sequelæ. Likewise, the character of the prevailing epidemic must be taken into account. In some epidemics a large proportion of the cases are mild, and the death rate is low. In other epidemics, or in some localities, the disease assumes a more severe form, and, in spite of the best treatment, the proportion that perish is much larger. A death rate as high as 60 per cent. has been reported; while in very mild epidemics it has been as low as 5 to 10 per cent.

It is a question whether *social status* and *domestic surroundings* have as much to do in determining the character of the disease as is generally supposed. It is true, however, that when diphtheria breaks out in an institution for children, especially foundlings, it is apt to be attended with great fatality. In our experience the patients sent to the hospital from careless and indigent families are not more liable to suffer from severe diphtheria than those which come from better and more sanitary homes. Nor do we find that delicate children perish in a larger proportion than the robust. In speaking of the influence exerted by social status, Lennox Browne says it has appeared to him "that when diphtheria attacks members of the upper classes it is often more malignant, and runs a more quickly fatal course than among the indigent; the disease finding, as it were, a more receptive soil in the case of those delicately nurtured than in those whose systems are in a manner accustomed to insanitary influences. On the other hand, and for obvious reasons, recovery from the sequelæ, when once the acuteness of the attack has passed off, is more expeditious and complete in the well-to-do."

There can be no doubt, however, that when diphtheria is at all severe, unsanitary surroundings would contribute toward an unfavorable prognosis. The less adequate the facilities for caring for the patient and the poorer the service, the greater are the probabilities that the disease will spread and increase in virulence. Where no attention is paid to ventilation of the sick-room, the vitiated condition of the atmosphere tends to lower the resisting power of the patient, and thus diminishes the chances of recovery.

Idiosyncrasy, or any family susceptibility to diphtheria that may be known to exist, should be taken into consideration as affording important prognostic data. Every practitioner knows how fatal the disease is in some families. It is worthy of notice that when diphtheria breaks out in a family, or in a neighborhood, children are almost always the first to be attacked, showing that in them the susceptibility to the disease is most marked.

Age.—There is not only an age disposition to diphtheria, but there is also an *age mortality*, and this must be taken into account in a forecast of the disease. The vast majority of all deaths from this affection

occurs among children under five years of age, and the mortality rate at this age period is vastly higher than in any other quinquennial period of life. This statement is confirmed by the statistics of all large hospitals for the treatment of diphtheria patients.

The following table shows the mortality, according to age, in the Asylums' Board Hospitals, London, 1892-93:¹

Age.		Admitted.	Died.	Percentage
Under one year	{ 1892	49	31	
	{ 1893	40	27	
		89	58	74.4
One to two years	{ 1892	106	66	
	{ 1893	166	106	
		274	172	62.7
Two to three years	{ 1892	163	90	
	{ 1893	219	121	
		382	221	57.6
Three to four years	{ 1892	193	96	
	{ 1893	296	146	
		491	245	49.9
Four to five years	{ 1892	240	106	
	{ 1893	320	142	
		579	249	43.0
Five to ten years	{ 1892	631	163	
	{ 1893	880	233	
		1511	396	26.2
Ten to fifteen years	{ 1892	209	16	
	{ 1893	296	20	
		507	45	8.8
Over fifteen years	{ 1892	414	16	
	{ 1893	610	36	
		1024	52	5.0

Of 1000 consecutive cases of diphtheria observed by Lennox Browne the age mortality was as follows:

Age.	No. of cases.	Deaths	Percentage.
Under 1 year	11	5	45.45
1 to 2 years	71	46	63.38
2 " 3 "	85	34	40.00
3 " 4 "	117	54	46.15
4 " 5 "	118	43	36.44
5 " 6 "	106	34	31.48
6 " 7 "	84	24	28.57
7 " 8 "	57	9	15.78
8 " 9 "	31	11	35.48
9 " 10 "	38	5	13.15
10 " 11 "	29	8	27.58
11 " 12 "	20	0	
12 " 13 "	16	0	
13 " 14 "	22	2	9.00
14 " 15 "	15	2	13.33
Over 15 "	178	7	3.93
	1000	283	28.3

¹ Lennox Browne, *Diphtheria and its Associates*.

Classified according to quinquennial age periods, the cases in the above table show as follows:

Age.	No. of cases.	Deaths.	Percentage.
Under 5 years	402	181	45.0
5 to 10 "	318	83	26.1
10 " 15 "	102	12	11.7
Over 15 "	178	7	3.93
	1000	283	28.3

In the following table of statistics, including over 9000 cases of diphtheria which were treated in the Municipal Hospital, Philadelphia, during a period of ten years, from 1893 to 1902, inclusive, the number of patients and the mortality rate within certain age periods are shown:

Year.	Under 1 year.			1 to 5 years.			5 to 10 years.			10 to 15 years.			15 to 25 years.			25 years and upward.		
	Admitted.	Died.	Per ct.	Admitted.	Died.	Per ct.	Admitted.	Died.	Per ct.	Admitted.	Died.	Per ct.	Admitted.	Died.	Per ct.	Admitted.	Died.	Per ct.
1893	1	2	66.66	82	25	42.68	58	17	22.07	18	3	16.66	36	3	8.33	265	2	0.06
1894	16	2	56.25	218	98	44.95	120	36	30.00	31	6	19.35	52	3	5.77	285	4	7.14
1895	25	10	40.00	327	122	37.3	187	43	22.9	46	7	15.2	56	4	7.1	685	4	0.1
1896	32	14	54.54	404	124	31.68	276	35	12.68	71	5	7.04	49	1	2.04	365	3	0.83
1897	34	16	47.05	560	190	35.53	437	65	14.87	126	14	11.11	39	3	7.69	49	0	0
1898	42	20	47.61	652	200	30.68	447	66	14.76	93	8	8.60	47	2	4.25	49	0	0
1899	38	24	63.15	659	181	27.46	462	59	12.79	102	7	6.81	62	2	3.22	50	3	6.00
1900	46	21	52.50	585	192	32.77	473	71	15.01	117	7	5.94	90	4	4.44	52	1	1.92
1901	20	15	50.00	874	119	13.61	287	28	9.75	104	6	5.77	56	4	7.14	36	1	2.77
1902	38	12	31.57	805	97	12.06	169	25	15.72	40	1	2.5	38	2	5.26	26	0	0
	299	147	49.16	4076	1371	33.63	2901	445	15.33	750	63	8.4	570	31	5.43	416	20	4.81

Sex.—We see no reason why *sex* should exert any influence on the mortality rate, and yet according to our observation, as well as that of some other writers, the death rate among the males is almost constantly in excess of that of the females.

The following table shows the mortality, *according to sex*, of all cases of diphtheria treated in the Asylums' Board Hospitals, London, from 1888 to 1894, inclusive:¹

Sex.	Admitted.	Died.	Per cent.
Males	5,245	1677	31.97
Females	6,353	1839	28.94
	11,598	3516	30.31

The following table shows the mortality, *according to sex*, of 1000 consecutive cases of diphtheria observed by Lennox Browne:

Sex.	Admitted.	Died.	Per cent.
Males	533	162	30.39
Females	467	121	25.91
	1000	283	28.3

¹ Lennox Browne. Loc. cit.

The following table shows the mortality, according to sex, of all cases of diphtheria treated in the Municipal Hospital, Philadelphia, from 1893 to 1902, inclusive:

Year	Males.			Females		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
1893 . . .	91	29	30.85	123	23	18.72
1894 . . .	214	81	37.85	251	72	28.68
1895 . . .	315	83	26.4	391	107	27.3
1896 . . .	424	100	23.56	446	90	20.22
1897 . . .	698	147	21.11	659	153	23.21
1898 . . .	562	152	27.04	667	145	21.73
1899 . . .	641	129	20.08	732	126	17.21
1900 . . .	669	151	22.56	698	147	21.08
1901 . . .	418	94	22.59	473	80	16.91
1902 . . .	285	84	29.45	316	73	23.10
	4256	1040	24.43	4755	1067	22.4

Race.—Race seems to exert no influence over the death rate from diphtheria. At least this is true in regard to the white and colored patients. Some observers believe that the blacks are more liable to perish from the disease than the whites, but this is not in accordance with our experience, as the following table shows:

Year.	White.			Black.		
	Admitted	Died	Per cent.	Admitted.	Died.	Per cent.
1893 . . .	206	60	28.84	9	2	22.22
1894 . . .	434	144	33.18	31	10	32.26
1895 . . .	660	178	26.9	46	12	26.00
1896 . . .	898	188	21.03	31	7	22.58
1897 . . .	1217	281	23.08	70	19	27.14
1898 . . .	1177	289	24.55	52	8	15.38
1899 . . .	1304	262	20.09	69	13	18.84
1900 . . .	1309	286	21.84	58	12	20.68
1901 . . .	843	163	19.33	46	11	23.91
1902 . . .	567	129	22.75	34	8	23.52
	8557	1975	23.08	454	102	22.46

While it is impossible to predict at the onset of diphtheria the ending of any case, yet it may be said that when the inflammation of the fauces is mild and the pseudomembrane not extensive, with but moderate swelling of the lymphatic glands of the neck, the termination is usually favorable. When the exudation is limited to the tonsils the danger is not great; the vast majority of such cases recover without any untoward after-effects. On the other hand, if the inflamed surface be extensive, the pseudomembrane copious, the exhalations offensive, and the neighboring lymphatic glands and the adjacent tissue very much swollen, the patient's condition becomes perilous. It may be safely asserted that the danger is increasingly grave in proportion to the extent of surface involved and the copiousness of the exudation. The parts implicated in the diphtheritic process must also be taken into account in forming a prognosis. In Lennox Browne's analysis of 1000 cases of the disease, the mortality, according to the site of the exudate, was found to be as follows:

Site of membrane.	Cases.	Deaths.	Per cent.
Fauces (alone)	666	81	12.16
Larynx "	4	1	25.00
Nares "	2	1	50.00
Fauces and larynx	112	51	45.53
" " nares	165	106	64.24
" larynx, and nares	49	30	61.22
Membrane involving the buccal cavity and lips	6	2	33.33
Membrane involving the hard palate . . .	12	11	91.66

If the fauces alone are involved the patient has a fair chance of surviving the attack. But where the exudate forms in a thick mass on the hard and soft palates the danger becomes imminent. Sometimes, however, the membrane peels off quickly, leaving the parts quite free from ulceration, and recovery speedily follows, although paralysis, more or less marked, of the palatine muscles, is rarely absent. The chief source of danger in such cases is from the absorption of the toxins, giving rise to toxæmia and heart-failure.

When the nares are involved the prognosis should always be guarded. Very many if not the majority of the milder cases of nasal diphtheria recover, and also some of the severe ones. But it is not often that the disease is limited to the nares. If the nasal cavities show distinct plugs of exudate in conjunction with marked faucial involvement, as is usually the case, the child's condition should be viewed with grave apprehension. The foregoing table shows that the mortality from faucial and nasal diphtheria was as high as 64.24 per cent.

In the severe cases of diphtheria nasal involvement is commonly present. As the capillary bloodvessels are very superficial in the cavities of the nose, the slightest congestion or ulceration of the mucous membrane of this part is liable to give rise to troublesome hemorrhage. This of itself is sometimes a source of danger. But the greatest danger is from systemic poisoning, which is extremely liable to occur, since the lymphatics, which are very numerous in the submucous connective tissue of the nostrils, take up the toxins and convey them to every part of the system. This condition always involves great danger of death by asthenia, due to toxæmia and heart-failure. If recovery takes place, more or less paralysis, local or general, is quite sure to develop during convalescence.

The occurrence of middle-ear disease as the result of diphtheria is deemed of sufficient importance to warrant prognostic consideration. It is believed that the diphtheritic process not infrequently extends from the postnasal space through the Eustachian tube to the middle ear. The aural involvement may impair the hearing, but only in rare instances does it result in deafness. Likewise, in severe nasal diphtheria the infection may be conveyed through the cribriform plate to the brain, causing meningitis. In analyzing his 1000 cases of diphtheria, Lennox Browne says: "It may also here be mentioned that, in one case of nasal diphtheria, death ensued from meningitis, and no aural complication was to be found. This circumstance offers a not improbable explanation of the gravity of nasal diphtheria. For, not only do the

turbinals constitute an extensive and readily absorbent surface, but there is a liability to direct cerebral infection through the cribriform plate, as has been observed in regard to cerebrospinal meningitis in which the specific organisms have been found in the anterior meninges."

On the first or second day of diphtheria there is but little to be learned from the subjective symptoms that is of prognostic value. A little later, in the graver forms of the disease, one may often see in the facial expression of the patient something indicating the serious nature of the malady that presents itself for treatment. This appearance has been characterized as a "peculiar facial cachexia." The face is pale and sallow, often puffy, bloated, or slightly cedematous; the skin is smooth and shiny, a mucopurulent discharge issues from the nostrils, the facial outline is somewhat changed by the swelling of the neck, the eyes are clear and bright, but the expression is often that of indolence and apathy. When the attack is likely to prove fatal the face becomes livid or of a dusky, pallid hue; in case of nasal involvement blood may either ooze or flow freely from the nares, and, in malignant cases, petechiæ or ecchymoses may appear, not only on the face, but also on other parts of the cutaneous surface. Altogether the facial expression is that of profound blood poisoning, and death may be expected at any moment.

Only in the mildest forms of toxæmia is recovery possible. When the patient suddenly becomes extremely pale, vomits everything that is swallowed, and the first sound of the heart is found to be diminished in intensity or absent, and the pulse becomes feeble, slow, and irregular, or disappears entirely at the wrist, the fatal end is not far off. Often the little patient will utter a shriek, as if suffering from pain, and place his hand over the precordial region just as he is about to expire. In these cases death results from asthenia or heart-failure, due to profound systemic intoxication. When diphtheria terminates in this manner, it is usually in the second week of the illness.

Temperature.—The prognostic significance of the temperature has been, we think, overrated by most writers. With Lennox Browne we feel that "One is so accustomed to read and hear of the fever of diphtheria that we almost hesitate to declare our conviction—formed on personal observation and confirmed by others whose experience is much greater—that as regards fever there is little to speak of as compared with the acuteness of the constitutional disturbance characteristic of the disease."

If the temperature continues high after the first few days of the illness it is most probably due to the development of some complication. In the worst cases of diphtheria the temperature soon falls to near the normal point, and, as the disease progresses, often becomes subnormal. With the other symptoms of toxæmia present, the occurrence of algidity should be regarded as a fatal omen, as it indicates the approach of death by asthenia. In septic cases the temperature may continue high, or it may fluctuate as in most other septic conditions. This can readily be explained by the inflammation of the lymphatic glands of the neck

which always accompanies this form of the disease. The prognosis in this variety of diphtheria should be exceedingly guarded.

Pulse.—By carefully studying the pulse from time to time one may sometimes acquire information of considerable prognostic value. So long as the pulse is not too rapid, remains regular and of normal volume, the case is probably progressing favorably. But when it becomes very rapid and feeble, or slow and irregular, our gravest apprehensions should be aroused. The pulse rate as well as its volume is influenced more by the absorbed toxins than by the pyrexia.

A rapid pulse within certain limits is not necessarily unfavorable so long as it remains regular. But if it constantly grows more and more rapid, and becomes irregular in its rhythm and force, the prognosis is proportionately bad. If, with a frequent and compressible, or a slow and intermittent pulse, there is also subnormal temperature, a pale, puffy, apathetic, and cachectic face, the prognosis becomes most grave. In speaking of the prognostic value of the pulse in diphtheria, Sir William Jenner says: "An extremely rapid and feeble pulse is of grave import; a very infrequent pulse is of fatal significance."

This disturbance of the circulatory system means that the heart's function is affected by the action of the toxin on the cardiac nerves, and possibly also that the myocardium is undergoing some change through the influence of the poison. When the heart's action becomes slow and weak there is danger of clots forming in the ventricles or in the large bloodvessels connecting with the heart.

One of the special dangers to be feared in diphtheria is involvement of the larynx, giving rise to membranous croup. The disease may occur primarily in the larynx, but more often it begins in the fauces and extends into the larynx. The patient cannot be considered free from danger of the pseudomembrane extending into this part so long as the disease continues, but the liability of such an occurrence progressively diminishes after the first week.

The danger in membranous croup is twofold: first, from laryngeal obstruction, causing suffocation and death; and, secondly, from bronchitis or bronchopneumonia. Much may be done toward overcoming the first source of danger by operative measures, but even then the diphtheritic inflammation too often extends downward into the trachea, bronchi, and bronchioles, and not infrequently into the alveoli of the lungs, giving rise to bronchopneumonia. We believe that about one-half of the deaths we have seen in membranous croup resulted from the latter complication.

The prognosis may be favorably influenced to a considerable extent by promptitude in employing such measures as intubation or tracheotomy for relief of the laryngeal stenosis. If, after either of these procedures, the child continues to breathe easily and noiselessly, sleeps quietly, takes nourishment well, runs a temperature of not more than one or two degrees above normal, and has a good color, the chances of recovery are favorable. On the other hand, if the respirations are uneasy and noisy, the temperature continues high, a troublesome cough

with rales throughout the lungs appear, and the color of the patient shows that the blood is not properly decarbonized, the chances of recovery are slim.

Membranous croup is much less liable to be attended by toxæmia or followed by general paralysis than are most other forms of diphtheria. But these affections may occur in cases of membranous croup as the result of involvement of the fauces or nares synchronously with the larynx.

Renal Complication.—Renal complication is not often of much prognostic importance. The slight amount of albumin that is frequently present in the urine is of no great significance, provided that granular and hyaline casts are absent. But when these, together with a large amount of albumin, are found, and the amount of urine excreted is greatly diminished, the outlook is not encouraging. If suppression of the urine occurs, death from convulsions and coma, as the result of uræmic poisoning, would soon follow if relief were not promptly afforded. In our experience such a termination in diphtheria is rare.

The prognosis of diphtheria should be greatly qualified when it occurs coincidently with or as a sequel to some other infectious disease, like *scarlet fever* or *measles*. In patients suffering from the latter disease diphtheria seems especially liable to assume the form of membranous croup, probably because of the catarrhal affection of the larynx usually present in measles. In the year 1900, measles of a malignant type broke out in the diphtheria wards of the Municipal Hospital, Philadelphia, and the mortality assumed unduly grave proportions. Of 68 cases of diphtheria complicated with measles, 34 died, a death rate of 50 per cent. Indeed, any independent affection, however mild ordinarily, supervening on an attack of diphtheria may become inordinately severe in consequence of the changed condition of the blood and nervous system of the patient.

Diphtheritic Paralysis.—The danger from diphtheritic paralysis depends very much on the parts involved. So long as the vital organs of the body remain unaffected the prognosis is not unfavorable. Paralysis of the soft palate, however inconvenient it may be to the patient, is not fatal. Likewise, in the average case of multiple paralysis recovery may be expected. Even in the more extreme cases, if the heart's function and the respirations are not affected, the chances of recovery are fair, provided the patient receives proper attention during the critical period. When deglutition is impossible, life may be preserved by feeding the child through an œsophageal tube. Cardiac paralysis, which is most to be feared, often develops suddenly and gives rise to dangerous symptoms of heart-failure. It is liable to occur either early or late in the disease.

We have already mentioned the fact that multiple paralysis does not make its appearance until the fourth to the sixth week of the illness. This complication, as well as some others to which attention has been called, tends to keep the patient's life in danger for a long time. Even when a well-marked case of diphtheria is progressing favorably, it is not too much to say that the danger period is not passed until at least six weeks have elapsed since the beginning of the attack.

CHAPTER XIII.

DIPHTHERIA (*Continued*).

THE TREATMENT OF DIPHTHERIA.

SINCE antitoxin has achieved for itself so much credit as an immunizing agent against diphtheria, it would seem that it deserves first place among the prophylactic measures to be considered. So important, indeed, is the question of serum treatment, not only with reference to its power of preventing but also of curing the disease, that we have concluded to devote a special chapter to the subject. We find it most convenient, however, to consider the question of treatment of diphtheria in the following order: first, the hygienic or preventive treatment; second, the medicinal treatment; third, the specific or serum treatment.

Preventive Treatment.—As soon as the nature of the disease is known the patient should be separated as far as possible from the other members of the household. This is important even when the attack is ever so mild, as severe cases may result from mild ones. If the patient is to be treated at home the other children, if there be any, should receive an immunizing dose of antitoxin and should be immediately sent out of the house. If this is not feasible, they should be excluded from the sick-chamber and assigned to bed-rooms in the most distant part of the dwelling. Their hygienic condition should be looked after; at least they should be properly fed, regularly bathed, and provided with plenty of fresh air day and night. Their throats and nostrils should be examined every day, and as soon as anything abnormal is discovered the child should be immediately separated from the others and given suitable treatment.

One of the uppermost rooms in the house should be selected for the patient. It should be light and properly heated, and provided with facilities for obtaining ventilation without incurring the risk from draughts. An open fire-place, with at least a little fire burning, is a very desirable aid toward maintaining the purity of the air in the room. The most suitable temperature is 70° to 72° F. All unnecessary hangings, furniture, and the like, that are liable to retain the contagium, should be removed from the chamber. In the winter months, when the heated air of the room is usually dry, it may be moistened by steam, which, if deemed advisable, may be slightly impregnated with eucalyptol, or some other fragrant essential oil. This is more especially advisable when the patient manifests croupy symptoms.

If more than one member of the family be ill with the disease, care should be taken not to overcrowd the patients. Each patient should

be allowed at least 2000 cubic feet of air space, with an additional allowance for the nurse. The nurse should be instructed to keep the patients as quiet as possible; at least, so far as active bodily movements are concerned. When the heart is found to be weak, she should feed the patient by means of a feeding cup, and not allow him to rise or get out of bed under any circumstance whatever.

During the illness of the patient the privileges of the well members of the household should be restricted. They should be advised not to attend church nor public assemblages of any kind. The children, if there be any, should at once be required to leave school, and should not be readmitted until the family physician or some qualified sanitary officer certifies that the sickness has ended, and that the house has been thoroughly cleansed and disinfected. The isolation of the patient should continue until the diphtheritic exudate has disappeared, and the affected mucous membrane has become entirely normal. When possible, cultures should be made to determine the absence of the specific bacilli; if two successively negative cultures be obtained it may be considered safe to allow the patient to associate with the other members of the family, provided he has had an antiseptic bath and is dressed in clean clothing.

As the infecting principle of the disease clings to articles which have been used by the patient, or which have been in the same apartment, all such articles as are worthless should at once be burned. Only such books, toys, and the like, as may be burned at the termination of the illness should be allowed in the sick-chamber. All articles for the laundry should be steeped for some time in a disinfecting solution, such as two fluidounces of chloride of zinc, or four fluidounces of strong carbolic acid, to a gallon of water, and afterward boiled for half an hour. For the disinfection of woollen goods formalin may be used, but for efficiency there is nothing that equals superheated steam. All utensils used by the patient in eating or drinking should be purified each time by means of boiling water. The secretions from the patient's mouth and nose should be disinfected by receiving them into a strong solution of chloride of lime, or a mercuric chloride solution (1:1000), or some other equally powerful germ-destroying agent. Small pieces of worn cotton goods, or cheesecloth, may be used to receive such secretions, and should be destroyed at once by fire.

The nurse or any other attendant should wear clothing made of such material as can be readily boiled and laundered. Before associating with well persons she should take an antiseptic bath, washing her hair at the same time, and change her entire clothing. The physician also, should exercise care lest he himself may be the means of conveying the infection to others. He should not remain in the sick-chamber longer than is necessary to make a proper examination of the patient. Before leaving the house he should take the precaution to wash his face, hair, and hands; the latter should be held for a few moments in some antiseptic solution, as mercuric chloride, 1:1000. He should delay visiting another patient until he has spent some time in the open air, or, what

is better, changed his clothing. It is desirable for him to wear in the room a long rubber coat or linen gown, which should be kept hanging in the open air during the interval of his visits.

As the body of a patient who has died of diphtheria is still capable of transmitting the contagium, certain precautions in regard to it are necessary. An effort should be made to disinfect the body by thoroughly washing it with some powerful disinfecting solution. There is perhaps nothing more reliable than chloride of lime. Six ounces of this drug to a gallon of water makes a very effective germicide. The body should be wrapped in a sheet saturated with this or some other similar solution before it is placed in the hermetically sealed casket, and the burial should follow as speedily as possible, without, of course, a public funeral.

When the illness has terminated, either by recovery or death of the patient, the sick-chamber and every article it contains should be thoroughly disinfected. This may be accomplished by using formalin according to the directions given in the article on disinfection, or by burning in the room three to five pounds of sulphur to every 1000 cubic feet of air space, the room having first been made as nearly air-tight as possible. (See chapter on Disinfection.)

As already indicated, all washable goods in the room of the patient should be immersed in boiling water for half an hour, and then laundered. Woollen clothing, mattresses, pillows, carpets, and all other articles which cannot be laundered, should be so arranged in a room as to be thoroughly exposed to the influence of the formaldehyde vapor or the sulphur dioxide. When feasible, such articles as those last named should preferably be sent to a disinfecting station and exposed to superheated steam under pressure for thirty minutes. All picture-books, toys, and other things sent in for the amusement of the patient should be burned. After the room has been disinfected, cleansed, and the paper on the wall changed, it should be thoroughly aired, and, if possible, remain unoccupied for a few days.

As some of these requirements would be only indifferently carried out by the average citizen, the local sanitary boards should have authority to exercise supervision over dwellings in which diphtheria makes its appearance, and should be provided with the necessary means and facilities for eradicating the infection. The work of disinfection should always be conducted by a properly qualified sanitary officer, and, as it is done in furtherance of public safety, the public treasury should supply the means. In every large city a suitable disinfecting station should be provided for purifying without cost all portable articles, particularly such as cannot be conveniently or properly disinfected at home. Philadelphia and many other cities of this country are provided with such facilities.

In order to afford health authorities the earliest opportunity to apply any or all of the measures which have been here indicated for restricting or preventing the spread of diphtheria, every case of the disease should be promptly reported as soon as the diagnosis is determined. In some municipalities the physician in attendance on a patient is

required to give such notification—a requirement which, we think, is not unreasonable.

Another means of preventing the dissemination of diphtheria, as well as other dangerous communicable diseases, is to apprise the public of the particular house in which it is present. How to do this without exciting opposition is a problem not easy of solution. The means adopted in many parts of this country is to affix, in a conspicuous place at the entrance of the house, a placard announcing the existence of diphtheria within. While this is usually distasteful to the householder, it serves the purpose of preventing any one from incurring danger unwittingly. But whether this plan be adopted or not, the sanitary authorities should keep the premises under supervision, instituting visits from time to time by officers qualified and empowered to advise and direct the observance of proper sanitary precautions, and, if there be danger of non-compliance, to put in force more arbitrary restrictive measures.

Besides enforcing the preventive and restrictive measures which have been outlined, antitoxin should be administered as a prophylactic in households in which diphtheria has made its appearance.

Local Treatment.—With reference to the therapeutic indications in diphtheria, it is necessary to consider both the local and constitutional manifestations of the disease. According to the present views relating to the etiological and pathological connection between the local affection and the systemic condition, it is obvious that local treatment, especially at the beginning of the disease, is a matter of great importance. If it be true, as we believe, that the disease is produced by certain organisms which, when deposited upon the mucous membrane of the throat or nose, will commence to multiply, if the soil be favorable, and elaborate a peculiar and most virulent toxin which is conveyed by the blood to all parts of the system, it is reasonable to suppose that local treatment should prove of great service.

It would seem, therefore, that it should be the prime object in treatment to destroy those organisms as early and as quickly as possible. But how to do this effectually without inflicting injury on the parts invaded is a question not easy of solution.

The probability of the correctness of this view has prompted many practitioners to make use of heroic local treatment. Such caustic and irritating applications to the throat as nitrate of silver, sulphate of copper, and strong solutions of permanganate or persulphate of iron were formerly much in vogue, and are not without their advocates at the present day.

Even more active cauterants, like hydrochloric acid and nitric acid, have been employed with asserted benefit. Flint speaks of a medical friend of his with much experience, who was convinced that by the prompt and thorough application of nitric acid, if the part primarily affected can be seen and reached, the progress of the disease may with certainty be arrested.

Such severe local measures are objected to on the ground that they impair the continuity of the tissues, and thus facilitate the entrance into

the system of the poisons generated by the Klebs-Loeffler bacilli and their associates. Impairment of the tissues also facilitates extension of the pseudomembrane, for it is well known that the mucous membrane of the mouth, if not intact, is liable to become involved in the diphtheritic process. All caustic and irritating local applications are therefore to be condemned as being more harmful than beneficial.

In place of the cauterizing lotions, most physicians now prefer those which are supposed to have more especially an antiseptic effect on the diphtheritic exudate. The drugs which have been employed for this purpose are very numerous. Among the more efficient antiseptics that have been recommended may be mentioned carbolic acid, permanganate of potassium, sulphite of soda, subsulphate of iron, benzoate of soda, chloral hydrate, and chlorate of potassium. These have been used singly, or two or more have been combined. They are usually applied in a liquid form by means of a cotton swab, a camel's hair brush, or the hand atomizer. Good results have followed the employment at short intervals of mild antiseptic applications. Salicylic acid is said to be useful when applied in the form of a dry powder in combination with subnitrate of bismuth. It has been used also in the form of salicylate of sodium in solution (7 parts to 100 of water).

Solution of chlorate of potassa has for a long time enjoyed considerable reputation as a gargle. Oertel advises a spray of chlorate of potassa and salicylic acid in solution. But, he says, the most suitable remedies to meet the indication of opposing septic infection and general poisoning of the system are alcohol, freshly prepared and properly diluted chlorine-water (the gargle containing 15 to 30 per cent. of chlorine-water), a solution of permanganate of potash ($1\frac{1}{2}$ to $2\frac{1}{2}$ grains to the ounce of water), or of carbolic acid ($2\frac{1}{2}$ grains to the ounce of water). Where these cannot be borne he recommends a solution of oil of thyme in equal parts of spirits of wine and water. He says: "With these the patient has to rinse his mouth once or twice at least every hour, or where this is not easily possible, as in the case of small children, we must seek to cleanse the mouth and throat by the use of the syringe."

Oertel attaches much importance to his recommendation of combining the use of antiseptic gargles with frequent inhalations of hot vapor. He believes that by thus setting up a rapid and abundant suppuration the separation of the pseudomembrane is not only hastened, but that the bacteria are partly taken up by the rapidly forming pus corpuscles, and partly washed away by them with the assistance of the antiseptic mouth washes and gargles. He says: "According to the individual peculiarity in capacity of reaction will this separation occur more or less rapidly; and it will depend upon the height the disease has already reached whether the septic affection and general poisoning can be prevented and how far this can be done."

After all, it must be admitted that gargles are of questionable utility. They can be used only in older children and adults; when most artfully used they do not reach much beyond the oral cavity. At the best they never touch anything beyond the anterior pillars, or not more than a

small part of the tonsils. In severe cases gargles are objectionable, in that the patient is required to rise from the recumbent position when using them. They are to be recommended only at the beginning of diphtheria, or where the disease is of a mild character, and even then their use must be limited to patients old enough to perform the act of gargling.

Applications to the throat may be made most conveniently and efficiently with an atomizer or a syringe. Lennox Browne had specially designed for his use a syringe which consists of two tubes, one straight and the other more or less curved, with several small holes at the end, and attached to a large rubber ball. It may be introduced into the mouth behind the teeth, or, with the curved tube, back into the post-nasal space when it is desirable to reach the pharyngeal vault.

His choice as a topical remedy, next to lactic acid, is the biniodide of mercury, for the reason that it does not precipitate the serum albumin as does the bichloride. He advises its use either in the form of spray, or douche by means of a syringe, in a strength of 1:2000 to 5000 of water. He says the results of syringing the throat with a solution of bichloride or biniodide of mercury are certainly excellent.

This author recommends the following formulæ:

LOTIO HYDRARGYRI BINIODI.

R—Red iodide of mercury	gr. ¼.
Iodide of sodium	gr. ¼.
Water	℥j—℥.

Sig.—To be applied by a swab or an irrigating syringe.

LOTIO HYDRARGYRI BICHLORIDI.

R—Bichloride of mercury	gr. ¼.
Water	℥j—℥.

Sig.—For application by a swab or an irrigating syringe.

Either of the above solutions is equal to 1:2000, and may be still further diluted if deemed advisable. As it is probable that a part of the lotion will be swallowed, we recommend that, in children, a much weaker solution be used (1:5000 to 10,000).

In the employment of these solutions, as well as most others that are usually recommended, Lennox Browne advises that they be used at as high a temperature as can be borne, as thereby their microbicidal activity is increased. He also calls attention to the fact that both alcohol and glycerin, so often prescribed in combination with antiseptic throat washes, are said to interfere with the germ-destroying properties of both mercury and carbolic acid.

Loeffler's experience with certain local applications in diphtheria is interesting, both from a practical and scientific point of view. According to Lennox Browne, "He found that the bacillus of diphtheria may be killed in twenty seconds by perchloride of mercury, chlorine-water, carbolic acid, or a solution containing turpentine and carbolic acid. But it not being always practicable to keep these topical applications in contact with the diphtherial membranes for so long a time, he endeav-

ored to discover other substances capable of more quickly destroying the bacillus. In the course of his researches he found that sesquichloride of iron, dissolved in equal parts of water, or in the proportion of 1 to 2, as well as other preparations of iron, kills the bacillus with twice the rapidity. Having also noticed that certain essences, such as benzol and toluol, interfere with the development of the bacillus of diphtheria, he investigated their action on animals, and afterward on man. For the latter purpose he employed a mixture containing iron, toluol, and creolin or metacresol. Finding, however, that this solution produced a marked smarting sensation in the throats of children, he added to it menthol.

"A cotton tampon steeped in this solution is applied to the affected parts twice in succession for ten seconds, and this treatment is repeated every three hours, until all the local symptoms have disappeared, which ordinarily occurs within four or five days. While the affection is still local, it may be arrested in its course by this solution; bacteriological examination will show that all the bacilli in the membranes are killed. Loeffler reports that in 96 cases treated in this manner, three-fourths of which were shown by bacteriological examination to be true diphtheria, not a single death occurred."

Loeffler recommends two solutions, the formulæ of which are as follows:

LOEFFLER'S SOLUTION (1).

R—Menthol	10 grams.
Solve in toluol ad.	36 c.c.
Alcohol, abs.	60 c.c.
Liq. ferri sesquichlorid.	4 c.c.—M.

LOEFFLER'S SOLUTION (2).

R—Menthol	10 grams.
Solve in toluol ad.	36 c.c.
Alcohol, abs.	62 c.c.
Creolin.	2 c.c.—M.

Either of these solutions may be applied with a cotton swab to the diphtheritic patches every three or four hours in the manner mentioned above. It may be well to clear the throat of mucus by mopping it with cotton before making the application. It is advised that the applications be made a little more frequently in bad cases.

We have not used these solutions extensively, but have given them a fair trial without obtaining results anything like as favorable as those seen by Loeffler.

Jacobi says: "When the diphtheritic pseudomembrane is within reach, it should be either destroyed or disinfected. For that purpose one or two drops of a 50 per cent. solution of carbolic acid in glycerin may be applied once (not more than twice) a day, or of the tincture of iodine, or of a solution of 1 part of the bichloride of mercury in 100 or 500 parts of water, several times a day." But he calls attention to the fact that only a small part of the pharynx is accessible to such treatment, and that it is possible to apply it to only a small class of patients. He condemns in forcible language the indiscriminate use of strong appli-

cations to the throats of children. He says: "Smaller children will object, will defend themselves, will struggle. It takes many an anxious moment to force open the mouth; meanwhile, the patient is struggling, perspiring, screaming, and exhausting his strength. One may succeed in forcing open the jaws, then there begins the practice of making applications, of swabbing, of scratching off the pseudomembrane, of cauterizing, of burning. The struggling child will prevent the limitation of the application to the diseased surface. One cannot help injuring the neighboring epithelium, and thus the morbid process will spread. Instead of doing good, we have done harm; for, indeed, no local application can do so much good as the struggles of the frightened children do mischief. I have seen them die while defending themselves against the attempted violence, leaving doctor and nurse victorious and alive on the battle-field." Jacobi believes that a very good local effect may be produced by the swallowing of medicines which are at the same time disinfectants, digestible, and easy to take; that they should be given in small doses and frequently repeated. Of this class of medicines he mentions tincture of the chloride of iron, lime-water, solutions of boric acid, bichloride of mercury, or benzoate of sodium.

SOLVENTS.—For the destruction and removal of the pseudomembrane, certain agents known as solvents have been employed from time to time. Among the unirritating solvents may be mentioned alkalies, pepsin, trypsin, and papayotin. The agent that has been most largely used is, perhaps, lime-water, or steam from slaking lime. Its solvent action, if it has any, is due to its alkalinity, which, as J. Lewis Smith says, may be increased by adding sodium bicarbonate to it. From observing its effects in a considerable number of cases, this author recommends with confidence the following formula:

R—Ol eucalypti	3 ij.
Sodii benzoat.	3 j.
Sodii bicarbonat.	3 ij.
Glycerine	3 ij.
Aque calcis	℥j—M.

Sig.—To be used with the hand atomizer from three to five minutes every half hour, or with the steam atomizer almost constantly

The writer says: "This alkaline spray not only exerts a solvent action on the pseudomembrane, but also renders the mucopus thinner, less viscid, and, therefore, so changes its character by diminishing its viscosity that it is more easily expectorated."

As trypsin is an active solvent in an alkaline medium, J. Lewis Smith suggests that it may be added with advantage to the alkaline mixture just described. Indeed, this writer is inclined to believe that such a combination forms the best solvent mixture known. The pseudomembrane has been seen to dissolve and disappear quickly under the use of the following formula:

R—Trypsin	gr. xxx.
Sodii bicarb.	gr. x.
Aque destillat.	℥j.—M.

Sig.—To be applied frequently with the hand atomizer or a cotton swab.

Pepsin has been used as a solvent with varying results. It was recommended in diphtheria solely on theoretical grounds, and has proved to be of doubtful utility.

Some writers speak favorably of papayotin in solution as a solvent of pseudomembrane. Among these may be mentioned Rossbach, J. K. Bauduy (Jr.), and Jacobi. The drug is said to be readily soluble in 20 parts of water, and it is claimed by Rossbach that if a few minims be placed on the tongue every five minutes the membrane will dissolve in two or three hours. Jacobi has used it with fair results, applying the solution with a swab or the atomizer. He says he employed the drug many years ago in greater concentration to dissolve, after tracheotomy, the diphtheritic membrane in the trachea below the tracheal tube.

As already intimated, Lennox Browne gives lactic acid first place among the local applications. He believes its efficiency is due in a measure to the fact that an acid medium is inimical to the bacillus, but that its greatest merit is its power to disintegrate or digest false membrane. He makes this strong statement: "Truth to say, we have been so well satisfied with lactic acid that we have been loath to try any other local remedy. We have not found it injurious to contiguous healthy tissue—that is to say, wherever the epithelial layer is entire. Its action appears to be limited almost solely to unhealthy tissue, promoting its disintegration by a process analogous to that of digestion; there is, it is true, some circumferential inflammation, but as this is only of the degree of healthy reaction and leads to the outpouring of scavenging leukocytes, it is to be regarded as a desirable result."

This author advises that the lactic acid be applied pure, or rather of (British) pharmacopœial strength, by the physician at least once or twice a day, and that the drug, moderately diluted, be applied by the nurse every three or four hours until the membrane has disappeared. The following formula is recommended:

R—Lactic acid (P. B.) 1 part.
Distilled water 8 parts.—M.

Sig.—To be applied by the nurse or attendant every three or four hours with a cotton swab or the hand atomizer.

Our experience with the so-called solvents in diphtheria has led us to believe that they are not to be depended upon. They may act very well in the test-tube, but their digestive and solvent action is too feeble to be of much practical value during the short time that it is possible for them to remain in contact with the pseudomembrane in the throat. While the antiseptic mouth washes, gargles, and sprays are useful to a limited extent, yet their action is too feeble and intermittent to be of any great practical value. We have already expressed our disapprobation of caustic applications, and we agree with those who believe that nothing is to be expected from mere astringents. When we consider that the purpose or design of local treatment is the prevention of extension of the pseudomembrane, promotion of its separation, destruction of the bacilli, and the prevention of toxic absorption, we must

admit that of the various remedies recommended, some of which even vaunted as specifics, no one has stood the test of experience.

We would not be understood as discouraging local applications in diphtheria; on the contrary, we believe that when used with good judgment they may be of great service. We have but little confidence, however, in their power to accomplish to any marked degree the purposes mentioned above, although as cleansing agents they are very useful. Any unirritating antiseptic solution may be employed, but after all, quite as much may be accomplished with a warm normal salt solution. It should be the aim of the physician to keep the parts involved as clean as possible without taxing too much the strength of the patient. This may be best accomplished by irrigation, either with a syringe similar to the one devised by Lennox Browne, or with the ordinary fountain syringe. Swabs should not be used, except by the physician or trained nurse, and then only with great care.

At the very beginning of diphtheria, or even when the disease is simply suspected, the throat should be sprayed every hour, at least for a few hours in succession, with a mild and unirritating antiseptic solution, such as a 1 per cent. boric acid solution, diluted Dobell's solution, hydrogen peroxide with equal parts of water, or a solution of 1:4000 or 6000 of bichloride of mercury. Twenty-four hours will probably determine whether it is possible to prevent or limit the development of the exudation. If not successful, and the disease goes on to its fullest development, the same applications may be continued every hour or two for the purpose of cleansing the throat. As already mentioned, a warm normal salt solution will accomplish the same end. We now employ it almost exclusively. Park, consulting physician to the Willard Parker Hospital, New York, prefers, in older children and adults, irrigation with a warm solution of salt every hour or two, and also every three to six hours to irrigate with some antiseptic solution, especially 1:1000 of bichloride of mercury. The irrigation of the throat, he believes, is best carried out with the fountain syringe. In the Municipal Hospital of Philadelphia we were in the habit of spraying the throat every two hours with peroxide of hydrogen. So long as the fauces are covered with exudate this drug may be used without dilution, but when the exudate has thinned out very considerably, leaving the mucous membrane excoriated and irritable, the peroxide should be diluted with one or two or more parts of water. When the exudate has almost entirely disappeared, and the throat remains irritable, the following application is often useful:

R ₁ —Menthol	gr. x.
Oil of sweet almonds	℥ j.—M
Sig.—Apply in form of spray.	

An operative procedure consisting of removing the tonsils at an early stage of diphtheria has been recommended. Lennox Browne and his colleague, Mr. Percy Yakins, and also a few other writers, claim to have seen good results follow the operation.

The objections to this treatment are that the exudate is liable to reform on the cut surface and the adjacent parts; that the injury inflicted affords a fertile soil for the propagation of the bacilli, and that the exposed lymphatics will permit of ready absorption of the toxins. The procedure has not met with much favor, and we would strongly advise against it.

Nasal Diphtheria.—As diphtheria of the nose and nasopharynx is most dangerous, immediate and persistent local treatment should be adopted with the object of preventing, as far as possible, absorption of the noxious products. The treatment consists in frequent cleansing and disinfecting the nasal cavities. The remedies usually employed do not differ materially from those recommended in faucial diphtheria. The decomposing material and foul discharge should be washed away as fast as they form. In order to do this, it is necessary to irrigate the nose very frequently—often every hour, or every two hours, day and night. In severe cases with a profuse fetid discharge the nares should be kept clean, no matter how much the child resists. The little patient may be restrained without suffering any harm by rolling him up in a sheet. If much exhausted, the child should not be raised from the recumbent position during the cleansing process. Only bland solutions should be employed, such as boric acid (5 to 10 grains to the ounce of water), chloride of sodium (teaspoonful to a pint of water), or some other equally mild antiseptic solution. The nose wash should always be used lukewarm, and the more thorough the washing the better it is for the patient. Instillations with a small medicine dropper, so often used by physicians, are not sufficient. Nor will the atomizer convey a sufficient amount of liquid into the nasal cavities to accomplish the purpose aimed at. A small (not too small) blunt-pointed syringe will answer the purpose much better. If carefully used, there is perhaps no better irrigator than the fountain syringe. It should be held just high enough for the solution to flow without undue pressure, and thus obviate any possibility of injury to the middle ear. If the nose inclines to bleed, the irrigation should be very slow and gentle. But if the epistaxis be free and quite uncontrollable, as sometimes happens, the irrigation will have to be dispensed with. It may then become necessary to direct attention to the hemorrhage. Alum, tannic acid, Monsel's solution, and the like, may be used. We have frequently found it necessary to plug the nares. Lennox Browne says the hemorrhage may generally be arrested by syringing the nostrils with the following antiseptic solution at a temperature not less than 100° F.:

R—Chlorate of potassium	½ oz.
Bicarbonate of sodium	½ oz.
Borax	½ oz.
White sugar (in powder)	1 oz.—M.

Sig.—A teaspoonful dissolved in five or ten ounces of water at 100° F. and use with nasal syringe.

For the local treatment of nasal diphtheria many physicians prefer some of the more active antiseptic and disinfecting solutions, such as peroxide of hydrogen, permanganate of potassium, carbolic acid,

bichloride of mercury, and so forth. Peroxide of hydrogen is quite useful if it be properly diluted. It is very irritating to the mucous membrane of the nose, and will cause pain if not diluted with 8 or 10 parts of water. Carbolic acid has been used in solution varying from 1:1000 to 10:1000 parts of water. Care should be taken lest too much of this drug be swallowed. Permanganate of potassium has been highly recommended. It has been applied to the fetid nares with a cotton swab, in the strength of 1:250 of water, once or twice a day. For irrigation it may be used several times a day in a solution of 1:2000 to 1:4000.

For washing out the nares, as well as the fauces, bichloride of mercury in solution has many advocates. Its well-known power as a germ destroyer has led to its use. It would doubtless be more freely employed were it not for the danger incurred through its poisonous qualities. As young children always swallow some of the liquid that is injected into the nares, most physicians hesitate to use a solution which is so highly poisonous. The same objection holds good against its employment for irrigating the fauces. Among those who recommend this drug for washing out the nares may be mentioned Jacobi. He advises that 1 part of bichloride of mercury be mixed with 10 parts of chloride of sodium or chloride of ammonium, and that from 2000 to 10,000 parts of water be added to form a solution, which should be used freely. He says if moderate quantities of this weak solution of mercuric bichloride be swallowed while being injected no harm is done. For correcting the fetid odor from the nares, he recommends, besides some of the solutions already mentioned, creolin in a 1 per cent. solution.

After some experience with most of the nasal washes mentioned above, we have, for the last few years, settled down to the use of the warm normal salt solution almost exclusively. We find that it answers the purpose quite as well as any of the antiseptic washes, and that it has the advantage over some others of being perfectly safe and unirritating. We may add that we have used with benefit peroxide of hydrogen well diluted with lime-water.

Aural Diphtheria.—But little treatment can be applied to the comparatively rare form of acute median otitis of diphtheritic character other than what is suitable for that affection when it occurs ordinarily. As pain is not often complained of, the condition is usually not realized until a purulent discharge issues from the external meatus. Nearly all that can be done then is to syringe the ear with a warm solution of boric acid or some other mild antiseptic wash. At the same time the nose may be irrigated with a similar solution. It is advisable that Politzer inflation be also employed with the hope of clearing the Eustachian tubes.

The insufflation of dry powders into the ear is not considered advisable, as they are likely to form dry crusts which may prevent the escape of the purulent material. Extension of the suppurative action to the mastoid cells rarely occurs; but when it does occur surgical treatment applicable to that condition should be resorted to.

Ocular Diphtheria.—For diphtheritic involvement of the conjunctiva, fortunately rare, the eye should be irrigated frequently—say every hour—with a boric acid solution (ten grains to the ounce of water), or some other equally mild antiseptic solution. This will be found difficult when the eyelids are very much swollen; but an effort must be made to keep the pus from accumulating under the lids. Ice applications,

FIG. 98



Position of child during irrigation of throat and nose. (After Park.)

in the form of iced cloths, are always indicated at first; but later it may be better to use warm applications. A strong solution of nitrate of silver may be applied to the pseudomembrane on the palpebral conjunctiva if care be taken to neutralize the silver salt immediately with a solution of chloride of sodium.

According to Lennox Browne, Hermann, of Breslau, has employed very efficaciously hourly pencillings of the affected eyelids with a 5 per

cent. solution of benzoate of sodium, and declares that since he began to use this treatment no patient under his care with this form of diphtheria has lost an eye.

Paralysis of the muscles of the eye occurring as a sequel to diphtheria calls for no special treatment. It will almost always disappear entirely in the course of two or three months.

Constitutional Treatment.—As diphtheria begins as a local disease very little internal treatment is required at the onset. Constitutional disturbance, however, occurs early, partly as a result of the local disease, but more especially from absorption of the toxic products of the diphtheria bacilli and the associated organisms. The prostrating effects of this poison are well known. The indications for internal remedies may be stated as follows: To aid the system in the elimination of the poison; to reinforce the debilitated vasomotor system; to improve the quality of the blood; to combat the poisonous effects of the toxins; to sustain the vital powers; and, lastly, to conduct to a favorable termination the secondary affections that may arise.

At the outset of the disease it is well to administer a gentle purge. For this purpose there is perhaps nothing preferable to calomel. *Liquor ammonii acetatis* (U. S. P.) is useful, as it tends to increase the secretions of the skin and kidneys. Water may be allowed *ad libitum*. Small pieces of ice held in the mouth will often have a soothing effect on the inflamed and painful fauces. Should the temperature of the patient be high, no attempt should be made to reduce it by the internal administration of antipyretic drugs, especially the coal-tar products, as they are too depressing. It is better to trust to tepid bathing. Bathing has the additional advantage of keeping the function of the skin active. At this early stage there is no article of diet equal to milk. There is, however, no objection to beef-tea and broth.

As soon as the diphtherial character of the disease is recognized iron should be administered. For the past fifty years this drug has had the confidence of physicians in this country, as well as those in most of the European countries, and by many it is regarded as our sheet-anchor in the constitutional treatment of diphtheria.

The preparation of iron that has achieved the greatest reputation in this disease is the *tinctura ferri chloridi*. It is believed to have both a local and general effect. It should be administered frequently and in positive doses. A child of one year may take as much as a fluidrachm in twenty-four hours, and a child of three to five years from two to three fluidrachms in the same period of time. It should be administered every hour or two. Some writers advise that it be given every fifteen, twenty, or thirty minutes. It should always be given diluted with a little water, so that the dose is about a teaspoonful. The addition of glycerin makes the drug more palatable. One part of glycerin to three parts of water makes a very good vehicle. If there is too much dilution no local effect can be expected from the drug. As a rule, it is well borne by the stomach; but there are exceptional cases in which it is not tolerated at all.

Jacobi, after using this preparation of iron for many years, expresses great confidence in it. He feels sure he has seen many bad cases recover through its use. But he has met with some cases in which its action was not so satisfactory. He says: "Still, I have often been so situated that I had to give it up in peculiar cases. They were those in which the main symptoms were of so intense a sepsis that the iron and other rational methods of treatment were not powerful enough to prevent the rapid progress of the disease. Children with nasopharyngeal diphtheria, large glandular swelling, feeble heart, and frequent pulse, thorough sepsis, and irritable stomach besides, those in whom large doses of stimulants, general and cardiac, may possibly bring any relief, are better off without the iron. When the circumstances are such as to leave the choice between iron and alcohol, it is best to omit the iron and rely on alcoholic stimulants mostly. The quantities required are so large that the absorbent powers of the digestive tract are no longer sufficient for both."

J. Lewis Smith regards the ferruginous preparations as holding an important place in the treatment of diphtheria, and says the one which has stood the test of experience is the tincture of the chloride of iron. He believes it should be given in large and frequent doses, as five drops hourly to a child of three years. He thinks it probable that those who have not observed its good effects have treated unusually bad cases or have given the medicine in small and inadequate doses. The best vehicle, he says, is glycerin and water.

Some writers maintain that an effort should be made to saturate the system as soon as possible with this drug, and, with this object in view, recommend that it be given in as large and frequently repeated doses as the stomach will tolerate. Ferguson, according to the author last mentioned, believes that this preparation of iron when freely administered partially arrests the blood change in diphtheria, and he recommends for a child of ten years the following mixture:

R—Tinct. ferri chloridi ʒ j.
Syr. simplicis ʒ iij.—M.
Sig.—One teaspoonful hourly in water.

If the stomach cannot tolerate this dose, it is advised that half a teaspoonful be given every half-hour.

Prof. Joseph E. Winters,¹ of New York, says that he has administered to a child of eight years as large and frequent doses of the tincture of the chloride of iron as two drachms, in combination with glycerin, every half-hour for forty-eight hours with marked benefit. And J. Lewis Smith cites an instance in which a woman, aged twenty-two years, greatly prostrated, having an excessive amount of exudate in the throat, and a very fetid breath, took daily one and a half fluidounces of the iron for ten days. But, he remarks, "it is only in the most severe or malignant form of the disease, the form described by Sanné as septic phlegmonous, that such large doses are proper or are required." He

¹ Diphtheria and its Management, 1885.

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ves, as do most physicians of the present day, that in the average of diphtheria five drops given hourly is the proper dose for a of three years.

e have used in our hospital work for many years the ferric chloride in doses practically the same as those last mentioned; but we prefer to combine it with the bichloride of mercury, as in the following formula:

℞—Hydrargyri chloridi corrosivi	gr ½
Tinct. ferri chloridi	ʒ j.
Syrup. simplicis	ʒ j.
Aq.	q. s. ad ℥ ij.—M.

Sig.—For a child of three years, one fluidrachm in a little water every two hours.

The internal use of bichloride of mercury in the treatment of diphtheria is not new. It was employed in this country as far back as 1860, by Dr. Tappan, of Ohio, with asserted benefit. It has, however, been used more frequently of late years, since it has been shown to be one of the most active germicides in medicine. The accepted theory of the microbic origin of diphtheria has led to the employment of this drug by many practitioners in the belief that when given internally it penetrates all parts of the system, destroying all micro-organisms with which it comes in contact. But as diphtheria begins as a local disease and becomes a systemic affection later, not because the specific micro-organisms enter the circulation—for in only rare instances have they been found in the blood—but because of the absorption of their poisonous products, it, therefore, may be that the remedial power of corrosive sublimate is limited to its local effect upon the organisms in the throat and pharynx. Whichever way its influence is exerted, locally or constitutionally, it has been found by many physicians to be very useful in diminishing the virulence of diphtheria and increasing the chances of recovery.

Though this drug has been widely employed in diphtheria, and at times administered in what would appear to be dangerous doses, very few reports can be found of its toxic or injurious effect. Dr. Grant¹ administered to a child of four years one-half grain of corrosive sublimate every half-hour until six doses were taken, and then hourly during the remainder of the day, every two hours on the second day, and on subsequent days at longer intervals. Jacobi has also administered it freely, but not in such heroic doses as just mentioned. He states that an infant a year old may take half a grain every twenty-four hours—of course, in divided doses—for many days in succession, with very little, if any, intestinal disorder, and with no stomatitis.

While large doses may be justifiable in extremely severe cases, we believe that smaller and safer doses are sufficient for general use. We agree with J. Lewis Smith, who says: "In ordinary cases the following may perhaps be regarded as about the proper quantities which should be administered in divided doses in twenty-four hours: For a child of two years, gr. ¼ (gr. ⅛ every two hours); for a child of four years, gr. ½

¹ Quoted by J. Lewis Smith, *Cyclopedia of the Diseases of Children*, by Keating.

(gr. $\frac{1}{8}$ every two hours); for a child of six years, gr. $\frac{1}{3}$ (gr. $\frac{1}{8}$ every two hours); and for a child of ten years, gr. $\frac{1}{2}$ (gr. $\frac{1}{4}$ every two hours)."

Calomel.—Calomel as a remedy in diphtheria has its advocates. It has been recommended with the purpose of securing both its cathartic and alterative effects. It may be useful as a gentle cathartic at the beginning of an attack, but to continue catharsis after the disease is fully developed seems objectionable on account of its tendency to weaken the patient and increase the anæmia which so soon becomes manifest in all severe cases, whatever the treatment. Much more is claimed for it when administered in a fractional part of a grain at frequent intervals. Many physicians of ample experience recommend it very highly in doses of one-tenth to one-quarter of a grain, repeated every hour or two. Some advise that a fractional part of a grain in powder form be placed on the tongue every hour or two, or even more frequently, and allowed to disappear gradually. It is claimed that when given in this way it acts both locally and constitutionally. Its tendency to act on the bowels may be obviated by the administration of a little paregoric at proper intervals.

Potassium Chlorate.—Potassium chlorate has been used in the treatment of diphtheria for almost as long a time as the tincture of the chloride of iron. It was formerly more often employed than at present, but it still has many admirers. Its great efficacy in stomatitis has encouraged the belief that it is also useful in diphtheritic pharyngitis. But, as the results have been disappointing, and the action of the drug tends to weaken the patient and injure the kidneys, especially when administered in doses believed to be sufficiently large to be of service, it has, to a great degree, fallen into disuse. Jules Simon says that while it acts wonderfully well in stomatitis he has obtained no benefit from it in diphtheria. Its tendency to cause albuminuria and nephritis when taken in large doses is well known. Where death has resulted from an overdose of this drug the kidneys have been found greatly damaged.

Potassium chlorate in combination with the tincture of the chloride of iron was, a few years ago, almost universally regarded as the remedy *par excellence* in diphtheria. The following formula, with some variations in the proportion of the ingredients, was for a long time a favorite prescription with most physicians of this country, and is still used by many:

R—Potassii chlorat.	3 j.
Tinct. ferri chloridi	ʒ ij.
Acidi muriat. dilut.	gtt. x.
Syr. simplicis	ʒ j.
Aquæ	q. s. ad ʒ iv.—M

Sig.—One teaspoonful every hour or two hours in a little water.

A child of five years may take one-half of the above mixture in the course of twenty-four hours.

Dr. Thomas M. Drysdale, of Philadelphia, who has had considerable experience in the treatment of diphtheria, claims that chlorate of potash

is so efficacious as to be almost a specific in this disease. He employs it in large doses. To an adult he gives fifteen grains, and to a child of twelve years seven and a half grains, every two hours. In such doses he does not fear any deleterious effect on the kidneys. In laryngeal diphtheria he recommends the following formula:

R—Potassii chlorat. ʒ ij.
Syr. limonis ʒ j.
Aqua ʒ iij.—M.

Sig.—For a child under two years one teaspoonful, and for a child from two to ten years two teaspoonfuls, every half-hour in urgent cases.

After an extensive use of potassium chlorate in diphtheria, and failing to obtain the favorable results claimed for it, we have abandoned it entirely. We feel inclined to agree with that noted clinician of his day, J. Lewis Smith, who says: "From what is known of its action, it would probably be better to abandon its use in diphtheria, since it is a remedy of doubtful efficacy for throat affections. If it be employed, it should certainly be administered in small doses sufficiently diluted. If it be prescribed, it should not, I think, be in larger quantity than half a drachm in twenty-four hours for a child of five years."

Turpentine.—Turpentine has its advocates in the treatment of this disease. It has been employed both locally and internally, with the result, as some writers believe, of arresting the formation and spread of the exudation, and preventing the secondary toxic effects. Cases have been reported in which severe croupy symptoms quickly disappeared under teaspoonful doses of pure turpentine, and the patient, in one instance, recovered without tracheotomy, which was before thought necessary. The dose more commonly employed has varied from ten minims to a teaspoonful, one to three times daily, in milk, sweetened water, or gruel.

Good results have been reported from the use of this agent by men of large experience and good judgment, among whom may be mentioned Baruch and Jacobi. Dr. Llewellyn, of Washington, D. C., speaks favorably of the action of turpentine when vaporized and inhaled. Its supposed efficacy is attributed to the fact that it is antiseptic and germicidal in its action. J. Lewis Smith says he has employed the vapor of turpentine with apparently good results. The mixture he recommends for vaporization is as follows:

R—Acidi carbolici,
Ol. eucalypti 4d ʒ j.
Spts. terebinth. ʒ viij.—M.

Two tablespoonfuls of this mixture are added to one quart of water, which is placed in a shallow vessel with a broad surface, and maintained in a constant ebullition or simmering upon a gas or other stove. He thinks that the vapor thus generated, "in passing over the inflamed surfaces, which are the seat of the exudate, with every inspiration, probably produces more or less local disinfection, apart from the systemic disinfection which it may cause by entering the blood and

the tissues generally." We feel that such a result is scarcely to be expected from turpentine. As to its alleged efficacy in diphtheria, however, we are unable to speak from any personal experience.

Sodium Benzoate.—Sodium benzoate, for internal as well as local use, has been highly recommended by a number of writers. Dr. I. N. Love regarded it as efficacious in from five to fifteen grain doses. Some observers claim to have shown that it arrests the growth of microorganisms. According to J. Lewis Smith, Helferich, Graham Brown, and Sanné believe that it is a specific against the virus of diphtheria. Smith says: "On the other hand, M. Dumas, surgeon to the Hôpital de Cette, has not derived any marked benefit from its use, and Prof. A. Jacobi says that it does not deserve the eulogies bestowed upon it from theoretical reasonings."

Such drugs as pilocarpine, copaiba, cubebs, resorcin, hyposulphite of sodium, and many others, have been recommended from time to time, but none of them deserves any prominent place among the therapeutic agents useful in the treatment of diphtheria. Of the internal remedies to which prominence has been given we would consider most useful the tincture of the chloride of iron and bichloride of mercury. To these we would add strychnine, digitalis, and alcohol. But as diphtheria is a disease of variable type, we must treat each case according to the indications.

Strychnine.—Strychnine is useful to combat cardiac depression. It may be given combined with tincture of the chloride of iron, or it may be administered separately. It is often advisable to inject it hypodermically. The dose should be adapted to the age of the child, but the amount which children of tender years will bear without harm is astonishing, especially when in a condition of toxæmia. A child of three years will take $\frac{1}{100}$ of a grain every four to eight hours; in an emergency a larger dose will be borne.

Digitalis.—Digitalis is also of advantage when the heart action is weak. In case of irritability of the stomach, which always occurs in profound toxæmia, digitalin may be administered hypodermically. Strophanthus, sparteine, caffeine, and the like, are also recommended to combat cardiac failure. To a child of five years two drops and sometimes as much as four drops of the tincture of digitalis may be given every four hours, or from one to six drops of the tincture of strophanthus. In a great emergency one or two unusually large doses of these drugs may be administered, followed by the more ordinary dose at proper intervals.

Citrate of caffeine may be used in doses from $\frac{1}{2}$ grain to 5 grains. Jacobi says: "For subcutaneous injections the salicylate (or benzoate) of caffeine and sodium, which readily dissolves in 2 parts of water, is valuable for emergencies, in occasional doses of from gr. 1 to 5 (6 to 30 cgm.), in from 2 to 10 minims of water."

Alcohol.—There are but few other diseases which demand more imperatively the use of *alcohol* than does diphtheria. Mild cases will frequently do well without stimulants; but no case, however mild it may

seem to be, should be considered out of danger until recovery has taken place. In view of the well-known depressing effects of the poison of this disease, even mild cases should receive small doses of some stimulant. Severe cases require a very liberal amount of alcohol in some form; it should be commenced early in the disease by giving small doses at first, and increasing the amount as the indications for its use become more pronounced. Whenever the heart action shows any loss of force, or the first sound of the heart becomes less distinct, or pallor is noticed, or the patient's strength is declining, large and frequent doses of some active stimulant are required. It matters little how the stimulant is administered, whether plain or in the form of milk punch or wine whey, provided that sufficient is given to produce the desired effect.

Whiskey is more often employed, for the reason, doubtless, that good whiskey can be more easily obtained than good brandy. If whiskey disagrees with a patient brandy should be tried. Either of these stimulants may be administered in teaspoonful doses properly diluted, to a child of five years. In septic cases the amount of alcohol which a child may take without showing evidence of intoxication is nothing less than astonishing. In this type of diphtheria it is not unusual for a child of five years to take one teaspoonful or even two teaspoonfuls of whiskey every hour, making the daily amount ingested from three to six ounces. While alcohol is ordinarily contraindicated in albuminuria or nephritis, yet rather than lose the support of so important an ally in combating toxæmia, it should, nevertheless, be cautiously employed.

If the toxæmia be well marked, alcohol in doses however large will not save the life of the patient, but it may prolong it somewhat. When the heart's action begins to wane, it is difficult to restore it. We cannot recollect of ever having seen a patient recover when the pulse was once lost at the wrist. Hence, the great importance of beginning the use of alcohol early. If the stomach will not tolerate either whiskey or brandy a good wine should be substituted. We have found champagne useful when the stomach is irritable. Aromatic spirit of ammonia is a good stimulant, and may be used temporarily, if it be found more agreeable to the stomach.

Attention should be given to the *diet* of a diphtheria patient throughout the entire illness. In the acute stage of the disease all food should be of a fluid character, consisting of milk, beef-tea, broths, and the like. It may be necessary to peptonize these, though, as a rule, the digestion is not bad. Ice and iced drinks may be allowed. Should there be a craving after cold articles, cold junket, frozen custards, and frozen beef-tea may be given. Soft-boiled eggs are useful when the patient is able to take them. Later, corn-starch, rice pudding, bread and butter, fruit and vegetables may be added. As early as possible a full, liberal diet should be allowed.

In regard to the complications of diphtheria, we feel that but little time need be spent here in discussing their treatment. Adenitis, otitis media, bronchopneumonia, and nephritis are the more common com-

plications encountered, and they present no indications for treatment at all different than when these affections occur from other causes.

The paralysis of diphtheria, however, differs from the other complications, in that it is peculiar to the disease. It cannot be prevented; and drugs avail but little in hastening the cure. The most dangerous form is cardiac paralysis. It is well to anticipate this condition by keeping the patient quiet, and endeavoring to sustain the strength of the heart by administering digitalis, strychnine, alcohol, and other cardiac tonics. As we have already seen, cardiac paralysis often develops suddenly, and the patient may die before the physician can be summoned. The earliest symptoms of this affection should receive prompt attention. The patient should remain as quiet as possible in bed, with his head low. It is sometimes advisable to raise the foot of the bed slightly. He should remain in the recumbent position when taking food, water, or medicine. Under no circumstances should he be allowed to leave the bed to empty his bladder or rectum. Whiskey or brandy should be given in doses sufficiently large to be of service. If the stomach be at all irritable, champagne is to be preferred. In case of a sudden seizure of heart-failure, hypodermic injections of brandy should be administered. The hypodermic use of strychnine will also aid in sustaining the heart action. Ammonia, camphor, musk, and the like sometimes serve as useful auxiliaries. At the same time the general strength of the patient should be well sustained with a liberal amount of nourishing and easily digestible food, such as peptonized milk, beef-tea, broths, or some of the concentrated foods designed for invalids with feeble digestion. For large children and adults soft-boiled eggs are useful, unless the digestion be very feeble. When improvement takes place the physician should see that the patient does not get out of bed too soon.

For the multiple paralysis which follows diphtheria the patient requires sustaining remedies, such as iron, quinine, strychnine, and alcoholic stimulants. Particular attention should be given to the diet, as there is ordinarily marked debility and anæmia, with a feeble digestion. Beyond the employment of a sustaining treatment we do not believe that much can be done to hasten the cure of diphtheritic paralysis. Some physicians believe that they have derived benefit from electricity, but a large number speak doubtfully of its efficacy.

As strychnine is known to be efficacious in many other forms of paralysis, it is frequently employed on general principles for the neuroses of diphtheria. Some observers have reported good results from its use, while others question its utility, except as a tonic. Prof. Henoch, Reinard, and Gerasimow claim to have hastened the cure of diphtheritic paralysis by hypodermic injections of strychnine. This drug is said to have been employed in one case (a boy, aged three and one-half years) with marked improvement in the tonicity of the muscles within twenty-four hours after the first dose, which consisted of about $\frac{1}{8}$ of a grain, and this was repeated each day for fifteen days, when the patient was considered cured. In another case (a child, aged six years) a complete

cure is reported from hypodermics of about $\frac{1}{8}$ of a grain daily for seven days, followed by $\frac{1}{16}$ of a grain each day for twelve days longer.

We are not convinced that strychnine possesses any special value as a remedy in diphtheritic paralysis. It is our opinion that tonics and a sustaining diet will do more toward helping a patient through an attack than anything else. The paralysis is seldom permanent. We have never known it to be so. In most cases complete recovery takes place in from two to four months.

There is, however, one thing connected with the treatment of multiple paralysis of diphtheria which is of great importance. We refer to the care a patient should receive when unable to swallow. In all severe cases deglutition is difficult and sometimes impossible. It is necessary then to sustain the strength of the patient by nutritive enemata, or by introducing food into the stomach by means of an oesophageal tube. The latter is preferable, as it gives us a better idea of the amount of nourishment that is utilized. The patient should be fed every four hours, and with each feeding there should be administered also such medicine, stimulants, and the like, as may be required. It is not often that a patient has to be fed with the oesophageal tube for a longer time than two weeks. We recall one case of paralysis in which this means of feeding was employed for sixteen days. By holding the jaws slightly apart with the gag of the intubation set, it is not difficult to introduce the tube through the mouth into the stomach. The tube will slip down more easily if slightly oiled. If a patient be safely carried over the period of difficult or impossible deglutition, his chances of complete recovery may be considered very good.

Treatment of Laryngeal Diphtheria (Membranous Croup).

It is deemed most convenient to consider the treatment of laryngeal diphtheria under three heads:

1. Prevention.
2. The means of promoting the separation and expulsion of the pseudomembrane.
3. The adoption of such operative measures as will overcome the mechanical obstruction to respiration.

Prevention.—There is no certain way of preventing laryngeal diphtheria, unless it be to guard the child against exposure to the infection of the disease. But when diphtheria begins in the fauces something may be done in the way of diminishing the liability of the membrane extending into the larynx. We have seen that a mucous membrane which is inflamed or congested is thereby predisposed to the diphtheritic process. It is advisable, therefore, to guard the patient, as far as possible, against the development of a catarrhal affection of the larynx. As soon as faucial diphtheria is recognized, the physician should see that the child is placed in a room of equable temperature and free from draughts. If the case occur in the winter season, and the atmosphere of the room is warmed by dry heat, it would be well to moisten the air

by the addition of a little steam. It has been suggested that the steam be impregnated with eucalyptol or some other fragrant essential oil, but we do not think that this is of any great importance. Care should be taken not to overcharge the air of the room with moisture, as this would be more harmful than beneficial. In the summer months fresh air should be freely admitted, with precautions against draughts, and steam may be dispensed with.

Drugs are of no avail in preventing laryngeal involvement. Antitoxin may be of great service as a preventive measure, but we have seen the pseudomembrane in the fauces extend into the larynx on a number of occasions even after the administration of antitoxin.

Means of Promoting Separation and Expulsion of the Pseudomembrane.—When false membrane has formed in the larynx, constituting membranous croup, nature's method of effecting a cure consists in the gradual disintegration of the membrane, or its separation and expulsion. How this process may be best promoted has always been a problem difficult of solution. *Emetics* have been freely employed, and of these turpeth mineral was for a long time believed to be especially useful. But they can be of no service unless the membrane be in good part detached. The persistent use of emetics is objectionable on account of their depressing effect. When, however, a flapping sound is heard in the larynx, indicating the presence of partly detached membrane, an emetic should not be withheld except in cases of profound asthenia. The one selected should be of that class which excites prompt and efficient vomiting without producing prolonged nausea and depression. Among those to be preferred we would mention ipecacuanha, powdered alum, and sulphate of zinc.

Warm Steam.—For the purpose of hastening the separation of the false membrane in croup there is a general consensus of opinion in favor of the continuous inhalation of warm steam. This is frequently impregnated with an alkali, like lime, or with some mild antiseptic agent, like eucalyptol, the compound tincture of benzoin, or turpentine. But it is the steam upon which the chief reliance is placed. Oertel believes that the energetic use of hot vapor causes a rapid and abundant suppuration of the diseased tissue, until finally the pseudomembranous layer becomes completely detached from the rapidly regenerating tissue of the mucous membrane, and is expelled either piecemeal or in its entirety. He regards this as nature's process of resolution in favorable cases.

The inhalation of warm steam is undoubtedly at times of much benefit, but we are inclined to believe that this treatment is often carried to excess. When shut up in a tightly closed tent in which a basin of water is kept constantly boiling, the child receives not only a diminished supply of oxygen, when the blood is already suffering from an oxygen dearth, but his skin is kept bathed in moisture, and his clothing and bedding are constantly damp. The effect of such treatment is certainly depressing. Warm steam inhalation should therefore be employed with some care. Lennox Browne says that the bed should be curtained

and the hot vapor "brought near it by means of a steam-kettle, but the croup-tent bed, which gives the little patient a continuous vapor bath, is as unnecessary as it is depressing."

Slaking Lime.—Inhalation of the warm vapor which arises from slaking lime in water has been highly recommended as a remedy in membranous croup. The vapor thus generated, being strongly alkaline, is believed by some to act as a solvent of the membrane. Oertel found that when a piece of pseudomembrane weighing three grains was placed in lime-water it swelled up in fifteen or twenty minutes into a loose, flaky mass, which could easily be divided, and after from thirty to forty minutes was completely dissolved. The assumption that lime-water acts in the same way when inhaled in the form of vapor as it does in the test-tube is not, we think, borne out by experience. At any rate this treatment is not so frequently employed now as formerly.

Calomel Sublimation.—The inhalation of sublimated calomel has been extensively used for the last twenty years or more with some degree of success. It is said to act not as a germicide, but by hastening the separation of the pseudomembrane, through, possibly, an influence exerted both locally and constitutionally. We have employed it frequently, but with only indifferent results. The number of cases which were materially benefited was small. The method of using it is very simple. Place the child in an improvised tent, not so large but that it may be fairly well filled with the fumes. The calomel may be sublimated by placing it on a small fire-shovel containing a few hot coals; or it may be placed on a red-hot shovel, or on a piece of sheet iron or tin, or in an iron spoon, either of which can be heated by means of an alcohol lamp or a Bunsen burner. Eight or ten grains should be sublimated every hour, or at longer intervals.

The Internal Use of Mercury.—The internal or constitutional treatment of membranous croup is to be carried out on the same lines as in the other varieties of diphtheria. Mercury in some form has long been employed, and most physicians believe that it gives better results than any other internal remedy that has been recommended. Calomel is much used in small and frequent doses, to the extent of causing slight ptialism. Many practitioners confidently expect improvement as soon as this effect is produced. Dr. T. Clarke Miller,¹ of Massillon, Ohio, expresses great confidence in mercuric chloride in the treatment of all forms of diphtheria. He gives $\frac{1}{16}$ grain of calomel every hour for twelve to twenty-four hours, and then continues the same dose every two hours. He says: "If I find that the exudate has originated in or extended to the larynx, I use antitoxin at once. If the nose is involved seriously, it is well to use antitoxin, though not to the exclusion of the calomel. I would omit the antitoxin rather than the calomel." The bichloride, cyanide, and iodide of mercury have also been highly recommended by some writers.

¹ The Diagnosis and Treatment of Diphtheria, read at the Toledo Meeting of the Ohio State Pediatric Society.

It is a pleasure to quote so often an author whose articles on diphtheria are everywhere regarded as classic. We refer to Prof. Jacobi, who says: "For nearly twenty years I have employed the bichloride in doses of 1 mgm. (gr. $\frac{1}{80}$) or more once every hour. The smallest babies take one-fourth or one-third of a grain daily for days in succession. Almost never will a stomatitis follow, and no gastric or intestinal irritation, provided the dilution be in the proportion of at least 1:8000. An occasional slight diarrhoea may require the addition of a few drops of camphorated tincture of opium. I can repeat a former statement, that never before the antitoxin period have I seen cases of croup getting well in such numbers, either without or with tracheotomy or intubation, as when under mercurial treatment." We have already expressed much confidence in the mercurial treatment of diphtheria, including, of course, membranous croup.

Operative Measures.—If it be found that the laryngeal symptoms do not improve under the treatment recommended, but, on the contrary, become more and more marked, or if the patient be not seen until the symptoms of mechanical obstruction have become alarming, recourse must be had at once to operative measures. The operation which is necessary to overcome the difficulty is either tracheotomy or intubation. Formerly tracheotomy was universally employed, but of late years it has been almost entirely superseded, in this country particularly, by intubation.

Intubation.—This procedure is viewed more favorably, mainly because it does not require the use of the surgeon's knife. We all know how reluctantly parents give their consent to the operation of tracheotomy on their child. When this operation was the only means of overcoming the obstruction to the entrance of air through the larynx, it was too often postponed until the child was almost moribund, and, consequently, the results were discouraging. Intubation being a bloodless operation, and not requiring an anæsthetic, parents do not hesitate to give their consent to this procedure, and hence the lives of many children who suffer from membranous croup are now saved that would otherwise be lost. It is a matter of great importance that operative interference, whether intubation or tracheotomy, be not delayed too long. It is almost criminal to allow a child to die from suffocation without making an effort to save its life by resorting to one or the other of these mechanical measures. While intubation is to be preferred in most cases, it cannot always take the place of *tracheotomy*. A physician without experience in intubation would be likely to fail in the operation, and if no one possessing the necessary skill is available, he would be obliged to resort to tracheotomy. Or the latter operation may be preferred, or even become necessary, when the membrane extends far down into the trachea. In such cases the intubation tube will not afford relief. *Tracheotomy* may also become necessary when the intubation tube is repeatedly coughed up.

The procedure for relieving the stenosis of membranous croup by placing a tube in the larynx with its upper end below the epiglottis

was first adopted by Bouchut in 1858. But, as his devices were crude, and as the operation was deemed impracticable by his confrères, and even ridiculed by them, he was discouraged from pursuing farther his conception of intubation. It remained for Dr. Joseph O'Dwyer, of New York, to devise and perfect the instruments necessary for the operation, and to demonstrate beyond question the utility of the procedure.

O'Dwyer's work of devising the intubation tubes was begun in 1880, without, it is said, any knowledge of the previous experiments of Bouchut. It required, however, some four or five years of diligent experimentation before the set of intubation instruments, herein described, was evolved into its present state of perfection. The New York Academy of Medicine has in its possession a complete collection of all the instruments used by O'Dwyer in his long series of experiments. The collection is interesting as showing the various changes in the size, shape, and construction of the intubation tube in its evolutionary process.

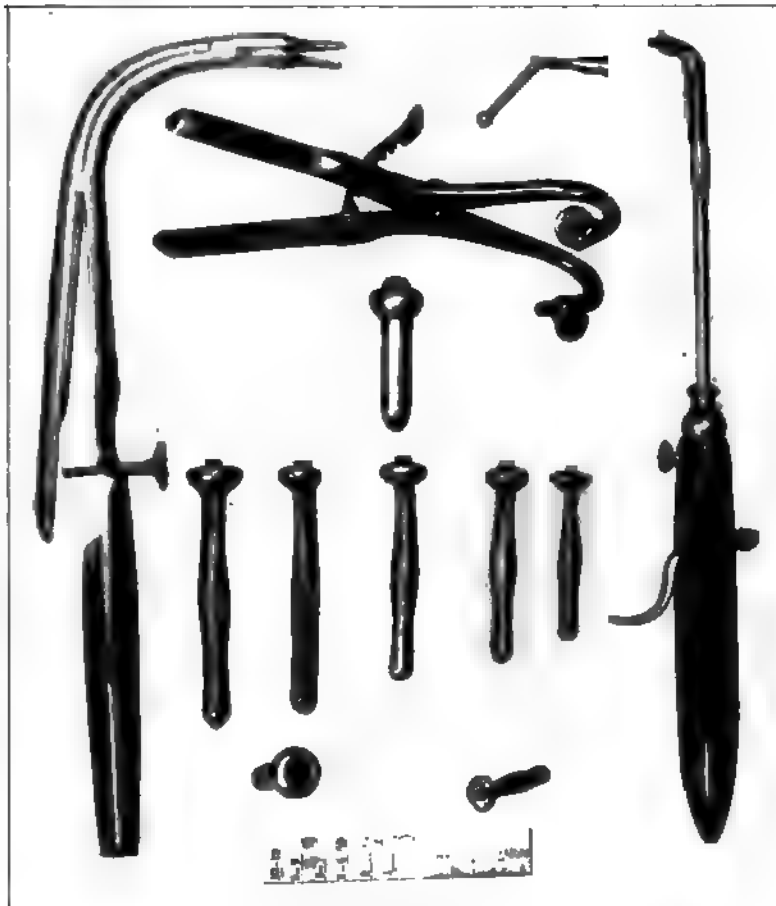
Intubation Instruments.—In their completed state the O'Dwyer intubation instruments consist of a series of *seven tubes*, a *scale* for measuring the size of the tubes, an *obturator*, an *introducer*, a *mouth gag*, and an *extractor*. The tubes vary in size, both as to their calibre and length, so as to fit the larynx of a child at any age. Tubes are also made suitable for adults, though they do not form a part of the regular outfit. The head of the tube is irregularly oval, with its anterior surface flush with the tube itself, so as not to interfere with the epiglottis, while posteriorly it projects backward so as to rest, when *in situ*, upon the *rima glottidis*. A tube that is too small for a patient may slip down into the trachea. In the left side of the head of the tube there is a small hole into which a string may be inserted. The object of this string is that the tube may be withdrawn in case it is introduced into the œsophagus instead of the larynx. The circumference of the tube is somewhat larger in its centre. The anterior and posterior surfaces of the tube are straight, while a central bulging is seen on either side. This is called the "retaining swell," as it helps to keep the tube in place, and to a great extent prevents its expulsion by the act of coughing. The lower end of the tube is rounded off and blunt, and its lumen throughout is elliptic (Fig. 99).

The tubes were originally made of white metal plated with gold; but later the inventor had them constructed of hard rubber overlying metal. This is considered an improvement, as the tube is much lighter, and more easily coughed out when the lumen becomes occluded with fragments of the false membrane. It is believed, too, that it is less liable to injure the larynx when worn for a long time. Certainly, it is less irritating from the fact that lime deposits do not form on it, as on the metal tube. The latter, when worn for a few days, is quite sure to become rough from these deposits. All intubation sets made at the present time contain only hard-rubber tubes.

Each tube is provided with an *obturator* which is fitted to the introducer. The obturator extends throughout the lumen of the tube,

projecting slightly from the lower end, where it is rounded or almond-shaped. It is divided into two parts, joined together by a hinge, which makes its removal easier after the tube has been introduced into the larynx. The obturator is either screwed fast to the introducer, or else it forms the terminal part of a long steel rod bent at a right angle, and so constructed as to fit the introducer. The latter construction of this instrument is now preferred by most operators (Fig. 100).

FIG. 99



O'Dwyer's intubation instruments. (After Park.)

The *introducer* is designed to facilitate the introduction of the tube. It contains the obturator, and is provided with a mechanical device for pushing off the tube after it has been placed into the larynx.

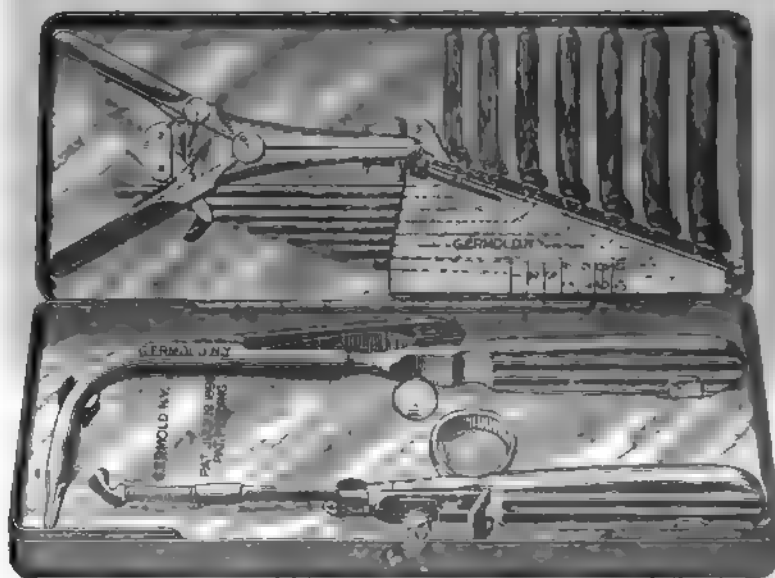
The *extractor* is an instrument curved at one end so as to form almost an angle of ninety degrees, terminating in a beak-like process which fits the opening in the tube. Its mechanical design is such that by pressing

a lever, the beak, which is composed of two parts, separates. When the beak is introduced into the lumen of the tube, and its jaws are separated by pressing the lever, the tube is grasped in such a way as to permit of its extraction.

The *mouth gag* serves the purpose of keeping the patient's jaws apart during the operation of intubation or extubation.

Short Tubes.—Besides the tubes described above, special tubes have been devised for the easy expulsion of loose membrane. They are short, reaching just below the cricoid cartilage. They are cylindrical, and have no retaining swell. Their lumen is large enough to permit pieces of detached membrane of considerable size to pass through. These tubes are believed to be of temporary service when there is a

FIG. 109



Latest design of intubation instruments. (After Northrup.)

good deal of loose membrane in the trachea. We cannot speak of their utility from personal experience.

Various modifications of the O'Dwyer instruments have been suggested from time to time, but most of them are unnecessary and some worse than useless. We can think of only one change that seems worthy of mention. Seeing that operators, especially those unskilled, often find it difficult to remove the tube from the larynx, and that the neighboring soft parts are frequently injured during the efforts at extraction, Dillon Brown, of New York, was led to modify the tube and devise a different extractor. His modification consists in attaching to the head of the tube a stiff wire loop which may be caught by the extractor. The latter instrument is a simple hook fastened to the end of the index

finger. He claims that this extractor not only greatly simplifies the removal of the tube, but makes it impossible to do any damage to the larynx during this procedure.

When this device was first brought to our notice we gave it a trial in the hospital, but it did not prove satisfactory. It is true that an inexperienced operator usually finds it difficult to remove the tube with the O'Dwyer extractor, but when the necessary skill has been acquired it can be removed readily with this instrument, and without any injury to the larynx. Northrup¹ says: "The extractor perhaps has called forth more censure than the other instruments. To quote the inventor: 'This cannot be improved upon except by inventing an instrument which will find the hole automatically.'"

The Indications for Operative Interference.—When operative interference is required, intubation, as already mentioned, is the operation to be preferred. But whether it be intubation or tracheotomy the indications for operation are the same. If, in spite of the treatment which has been recommended for membranous croup, there is progressive asphyxia, as evidenced by increasing dyspnoea, labored breathing, stridor, suppression of voice, cyanosis, retrocession of the supraclavicular fossæ, as well as of the epigastrium and the lower ribs, the operative procedure should not be delayed.

Intubation is not so simple an operation as to be resorted to indiscriminately. When introduced, the tube acts, of course, as a foreign body in the larynx and is not incapable of doing harm. To say nothing of the slight abrasion that may result from its introduction, even by skilled hands, its presence in the larynx for several days is liable to cause ulceration at the points where it impinges. But, notwithstanding this fact, when the indications for intubation are clear and unmistakable it should be performed at once. Do not wait until the pulse begins to flag and the child's strength becomes exhausted, else death may suddenly occur from heart-failure. We repeat that when there is a marked retrocession of the epigastrium at each inspiratory act, and cyanosis is evident, intubation should not be delayed another moment. By waiting longer nothing but harm can come to the lungs and to the heart.

The Technique of Intubation.—No anæsthetic is required for this operation, but it is necessary that the child should be brought under perfect control. This may be accomplished by placing the child's arms downward in a straight line with the body and rolling him up in a sheet or light blanket. In thus preparing the child care should be taken to avoid having too great a bulk of the blanket on the chest of the child, as this will interfere with the manipulations of the operator. The child should then be placed on the lap of a nurse seated in a chair, with its head somewhat above her left shoulder. She should grasp the child in her arms, and hold its legs firmly between her knees. (See Fig. 101.) The child is thus brought under complete control, with no great increase to its discomfort.

¹ Nothnagel's Encyclopedia of Practical Medicine, American edition.

The gag should now be placed between the jaws of the child on the left side, and held by the assisting physician or nurse, who, standing behind the child, steadies also its head with a firm grasp of his hands. It is assumed, of course, that the operator has already selected the tube suited to the age of the child, that he has inserted into the eyelet of the tube a silk ligature or string, which, when both ends are tied together, is long enough to reach nearly to the end of the handle of the introducer, and that he has affixed the obturator with its tube to the introducer. It is advisable to see that his instruments work well by pushing the tube off of the obturator once or twice before beginning the operation.

FIG. 101



Showing the first steps of intubation in the upright position

All preliminary arrangements being completed, the operator, sitting or standing, as he may prefer, in front of the patient, inserts his left index finger and feels for the epiglottis. Having secured it, he pulls it forward on the base of the tongue, keeping his finger as much to the left as possible. With the introducer in his other hand, he passes the tube over the dorsum of the tongue until it reaches the chink of the glottis, when the handle of the introducer should be quickly raised so that the tube may pass downward into the larynx. It should then be pushed off and the obturator withdrawn, the tip of the finger meanwhile being held on the head of the tube to prevent its being pulled out. The operator should not let go the string until he is sure the tube is in the larynx. Its presence in the larynx is known by the shrill metallic

cough, and by the relief of the dyspnoea. If the tube has been introduced into the oesophagus there is, of course, no relief. This location of the tube may also be recognized by the fact that the string grows shorter as the tube descends into the oesophagus. It should be pulled out at once.

The tube being properly placed, it is well to remove the mouth gag and allow the child to cough and expectorate for a minute or two, and at the same time to be sure that there is no obstruction in the tube. Everything being satisfactory the gag should be reintroduced, the string cut and withdrawn, while the tip of the index finger rests on the head of the tube to prevent its displacement. The child should then be released and put to bed.

If the child is very young, having no molar teeth, and the operator distrusts his ability to remove the tube with the extractor, the string, instead of being cut and withdrawn, may be looped over the ear of the child and secured to the cheek with a strip of adhesive plaster. In this case the hands of the child must be muffled, else the offending string will be caught with the fingers and the tube pulled out. In children with teeth this procedure is not to be recommended, as the string is soon chewed off and rendered useless. Experienced operators, however, prefer to remove the string in all cases.

There are still some other points in connection with the operation that the beginner should know. In the first step of the operation the operator's hand containing the introducer should be close to the chest of the patient. The tube should be pushed backward on the median line of the tongue until it reaches the chink of the glottis, then the handle of the instrument must be raised, and the tube should slip down into the larynx without much force being used. The tube, during its introduction, sometimes causes a slight spasm of the parts, in which case the operator should pause for a few moments, when the spasm will probably relax and the tube slip into place. It should be remembered that the epiglottis must be kept out of the way; if not the operation will surely fail. It is important, too, that the child should be under perfect control in the arms of the nurse, and that it should squarely face the operator. The position of the child's head and neck should be, as Northrup says, as if the child were suspended from the top of its head.

In case the first attempt at placing the tube is unsuccessful, rather than exhaust the patient with repeated trials at one sitting it is better to remove the gag and allow the child a few seconds to rest, or to cough and expectorate. A beginner rarely succeeds the first time; it is far better that he should make several short attempts than a prolonged one.

A vigorous cough following the introduction of the tube is favorable rather than otherwise, as it shows that the parts have not lost their sensitiveness, and it clears the mucus from the trachea. If there is no cough, and the breathing ceases and the cyanosis deepens, there is surely an obstruction at the lower end of the tube; in which case it

should be removed immediately. If the same result follows a repetition of the operation, tracheotomy should be performed.

Some operators prefer to have the child in the recumbent position during the act of intubation. The advantages claimed for this position are that the operation can be performed with but a single assistant, and that there is less danger of heart-failure if the patient be greatly prostrated. The child should be rolled up in a sheet or thin blanket, as already described, and placed squarely on its back. See Fig 102. In other respects the operator should proceed as before. At the present time the resident physicians in the Municipal Hospital employ this method altogether. It is also employed in the Willard Parker Hos-

FIG. 102



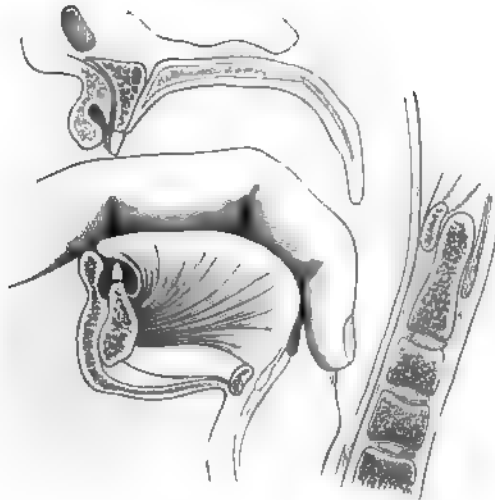
Showing the first steps of intubation in the dorsal position. Photographed by Dr. B. Franklin Royer.

pital, New York, and is recommended by Casselberry, of Chicago, and Carstens, of Leipzig.

Dangers and Difficulties of Intubation.—The operation cannot be said to be dangerous when performed by an experienced operator. It is true, instances have occurred in which exudate has been pushed down into the trachea by the tube, causing suffocation and instant death. This condition, however, is easily recognized at once, and the prompt removal of the tube is usually followed by forcible expulsion of the detached mass of false membrane. When this occurs the dyspnea may be so greatly relieved that reintubation is not necessary. But frequently the membrane reforms and the operation is again called for.

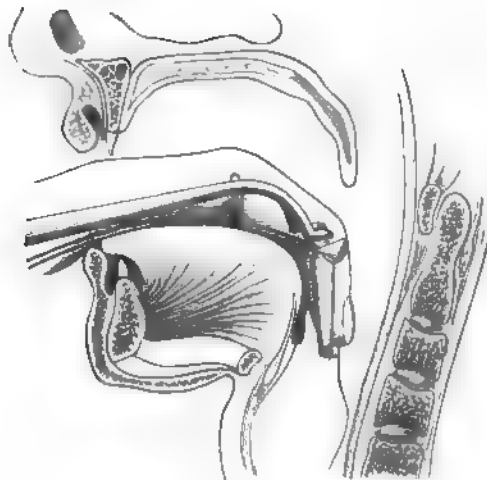
Under the circumstances just mentioned, we would emphasize the importance of removing the tube promptly; for if there is too much delay the sensitiveness of the parts soon becomes so blunted that cough,

FIG. 103



Fixation of the larynx. (Lejars.)

FIG. 104



The tube guided by the index finger (Lejars.)

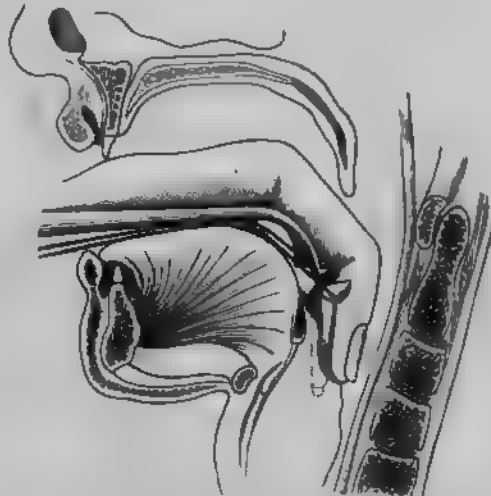
on which the safety of the patient depends, is not excited, and death speedily results from suffocation.

The inexperienced and clumsy operator may incur other dangers, such as asphyxia from prolonged attempts at intubation, lacerating the

tissues, or forcing the tube into a false passage. All of these accidents can be avoided with care.

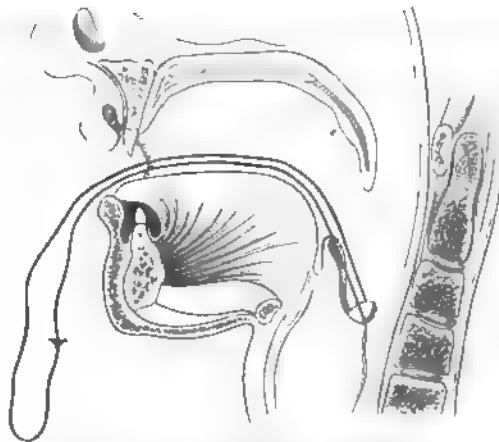
There are but few serious difficulties liable to be encountered by the experienced operator. It has been said that the tube may be

FIG. 105



The tube penetrates the larynx. (Lejars.)

FIG. 106

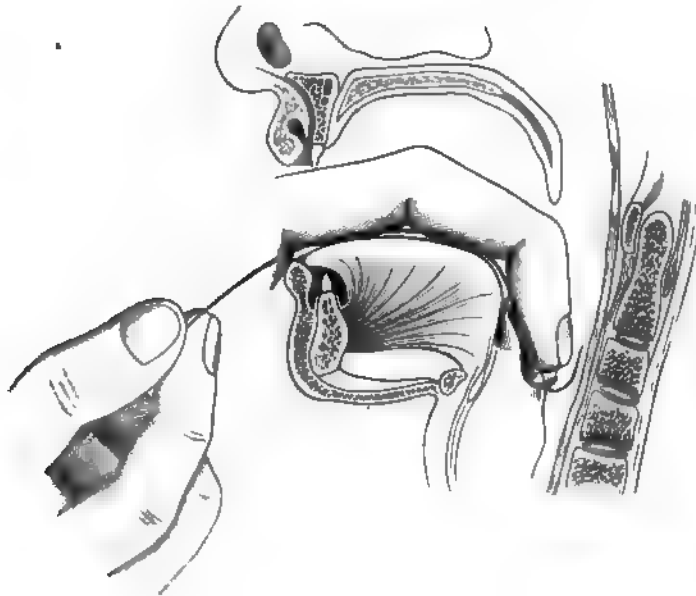


The tube in its proper position (Lejars.)

obstructed in its course by entering one of the ventricles of the larynx. This, we are sure, hardly ever happens with the O'Dwyer tubes which are so nicely rounded at their ends. Besides the pushing down of membrane before the tube, or the occurrence of a slight spasm of the

muscles of the larynx, as described above, in introducing the tube the operator will sometimes meet with difficulty caused by swelling, inflammatory thickening, or oedema of the subglottic tissues. When it is found that the tube adapted to the age of the child will not enter readily, it is advisable to try a smaller one. After this has been worn for a short time there is usually no difficulty in introducing one of the proper size. The narrowest part of the lumen of the larynx is in the region of the cricoid cartilage. We have seen a few instances in girls in which the cricoid ring was abnormally small, a fact which we have been able to demonstrate *post-mortem*. When this condition exists only a little swelling or oedema of the lining membrane is needed to make the intro-

FIG. 107



Withdrawal of the thread. (Lejars.)

duction of the tube difficult. The only thing to do in such cases is to use a smaller tube.

Treatment and Feeding After Intubation.—It is advisable not to make any local applications to the throat while the tube is in the larynx; at least, irrigation or spraying should not be practised. The applications to the nose, if required, need not be omitted. Internal treatment, stimulants, and the like, may be continued as before.

The feeding of the child is the thing that frequently gives us the most concern. Some children swallow with but little difficulty after intubation, while it is really distressing to see others drinking liquids of any kind. The act of swallowing excites coughing, and this may be still further excited by some of the liquid running down the tube into the

trachea. The cough is often violent, causing a large part of the liquid in each act of swallowing to be forcibly expelled, not only through the mouth but through the nose also. Children, however, usually persevere in drinking, and after a little while they frequently get along better. Semisolid food is not so liable to cause coughing, and is, therefore, preferable. When a child is old enough, we prefer to have it fed on bread soaked in milk. This forms a bolus which can be swallowed, as a rule, without exciting much cough.

FIG. 108



Casselberry's position for feeding intubated cases (After Northrup.)

It is claimed that the difficulty of swallowing, even of liquids, may be overcome by placing the child on its back with the body and legs elevated, while the head hangs over backward at an angle of forty-five degrees or greater. It is thought that any liquid that may get into the tube will, with the child in this position, run out again rather than into the trachea. The placing of the child in this position during feeding was first recommended by Casselberry, of Chicago. He and many other physicians who have tried this method speak of it very favorably. In our experience it has not proved so satisfactory. In bottle-fed babies

it sometimes answers fairly well. It should be stated that some physicians believe that the child swallows better lying on the abdomen with the head hanging forward.

If it be found that the child is not getting sufficient nourishment by either of the methods mentioned, gavage should be resorted to. This may be done by introducing either a small œsophageal tube or a flexible catheter through the nose into the stomach. If this route is found inconvenient or difficult, the child's jaws may be slightly separated and the tube introduced through the mouth. If one catheter should not be long enough another may be joined to it by means of a short glass tube. Some prefer rectal feeding, but we have never found it satisfactory.

Removal of the Tube, or Extubation.—The time for removing the tube will depend very much on the age of the child and the stage of the disease. In older children the tube may be removed earlier than in those who are younger. Likewise, when the tube is not required until a late stage of diphtheria, it may be removed sooner than when introduced at an early stage of the disease. We have seen it stated somewhere that O'Dwyer recommended that the average time of wearing the tube should be seven days; and if the patient's residence is a long distance from the physician's office the time had better be eight days. It has been our rule to allow the tube to remain in place six days before removing it. Frequently, however, the resident physicians remove it earlier, but they often find it necessary to reintroduce it. Northrup thinks that five days for a child over two years is long enough for the tube to be worn in the average case. He says: "At the Willard Parker Hospital the time allowed is four days; at the New York Foundling Hospital, three days." He, with many other writers, believes that the length of time which the tube is required in membranous croup has been materially reduced by the use of antitoxin; also, that reintubation is now less often required.

Cases are not infrequently seen in which the tube, after having been worn for only a short time, is coughed up and expelled, together with a mass of membrane. Such cases sometimes recover without reintubation being required. There are other cases in which the tube is not retained longer than it is needed; that is to say, in the course of four or five days, when the membrane in the larynx has disappeared and the œdema subsided, autoextubation takes place through the agency of the cough. This result is always gratifying, and especially so to the inexperienced operator.

Whenever the tube becomes obstructed it must, of course, be instantly removed. Fortunately, in most cases it is coughed up. When coughed up, the tube is either expelled or the child removes it from the mouth with his fingers. In rare instances it is swallowed. Should this occur, no great uneasiness need be felt, as we have never known a tube that was swallowed fail to pass through the intestines.

The Technique of Extubation.—Up to a certain point the technique of the operation of extubation is exactly the same as that of intubation. After being rolled up in a blanket or sheet, as before, the child should

be held in the upright position on the lap of the nurse, or placed in the dorsal position, according to the choice of the operator. It is equally important that the child's head should be held steady, and that the axis of the head, neck, and trunk should correspond. The mouth gag being in position, the operator passes his index finger of the left hand backward over the dorsum of the tongue until he feels the tube and determines its position. He should then tilt the epiglottis forward and control it. Holding the extractor in his right hand, with the handle of the instrument near the chest of the child, he should pass it backward along the side of the finger until the tube is reached; the handle of the extractor should then be raised to a horizontal position, and, with the aid of the tip of the finger which is controlling the epiglottis, he inserts the beak of the instrument into the opening of the tube. Having succeeded in doing this, he presses down the lever at the upper part of the extractor with his thumb, which causes the two parts of the beak of the instrument to separate, and thus the tube is caught and held, very much as a glove stretcher holds the finger of a glove. The operation is completed by lifting the extractor with the tube until it impinges on the hard palate, then depressing the handle and withdrawing the instrument and tube from the mouth. If the tube should slip off, as it often does, after having been lifted from the larynx, its removal can easily be concluded by means of the finger.

It is important to properly regulate the distance of separation of the two parts of the beak of the extractor. This may be done by means of the screw in the handle. If the jaws of the instrument are allowed to open too widely the orifice of the larynx may be lacerated by a clumsy operator. The extractor should be held in the hand lightly, as no great force is required to remove the tube. Be careful not to place the thumb on the lever until the beak of the instrument is well within the opening of the tube.

If the operator should have difficulty in grasping the tube, it is better to make repeated short attempts, allowing the child to rest for a minute or two in the intervals, than to make a single prolonged effort. As extubation is more difficult than intubation, beginners often become nonplussed in their efforts to extract the tube. In such a dilemma, enucleation, or removal by pressure, is recommended. Park¹ says: "It is possible in an emergency, in the majority of cases, to easily expel the tube by placing the child face downward with the body slightly elevated, and pressing gently against the trachea along its anterior surface, just below the end of the intubation tube." One of the writers tried this expedient a few years ago, but did not succeed. It was feared that the amount of pressure required to accomplish the purpose might injure the larynx.

After the tube has been removed the patient should be placed in bed and carefully watched for a while to see that the respirations continue easy. In family practice the physician should not leave the house for

¹ Loomis-Thompson, *American System of Practical Medicine*.

at least thirty minutes. If there is any difficulty in breathing he should remain until he feels reasonably sure that the patient is going to get along without the tube. Reintubation is often necessary. When dyspnoea returns after extubation the condition of the patient not infrequently becomes critical so quickly that if prompt aid be not afforded death from suffocation will surely result. It is, therefore, highly important that the physician should be within easy call for some hours. Having seen not a few children perish at this stage of the disease when their lives might have been saved by prompt aid, we feel that the importance of the advice just given cannot be emphasized too strongly. To lose a child during the height of an attack of membranous croup is bad enough, but to see it die after the danger has apparently passed, and when the brightest hopes are entertained for its recovery, is much worse. Such a result may not inaptly be compared to the sinking of a ship in the harbor after it has weathered the storms of the ocean.

For lessening the nervous excitability of the patient, as well as for its relaxing effect, a little morphine may be given just before removing the tube. Park says that at the Willard Parker Hospital, "immediately after the extraction of the tube, the child is given $\frac{1}{84}$ grain of morphine hypodermically, and an ice-bag is applied to the larynx. It is sought in this way to lessen the irritation and swelling of the larynx. The child is still kept in a recumbent position for one or two days." Perfect quietness at this time is of great importance. A few hours of quiet sleep after extubation is quite desirable, as it will sometimes tide a patient over the period at which the indications for reintubation are most likely to develop.

Prolonged Intubation.—Despite the free use of antitoxin, and the greatest possible care in the operation of intubation and extubation, it frequently happens that the tube must be worn for a much longer period than five or six days. In other words, when the tube is removed at the time just indicated, the dyspnoea returns, making reintubation necessary; and this sometimes happens over and over again in the same patient through a long series of intubations and extubations. We know of nothing connected with the work of intubation that is more perplexing to the operator, or more distressing to the patient, than this unfortunate occurrence. Some of these cases require months and in rare instances years of intubating until recovery takes place. Indeed, a large proportion of the most obstinate cases perish from one cause or another before the difficulty is overcome.

Prolonged intubation is not always due to the same cause; it may result from one of several causes, such as persistence of the false membrane in the larynx, oedema of the tissues, subglottic laryngitis with thickening of the soft parts, ulcerations, exuberant granulations, cicatricial contractions, destruction of the cartilages and collapse of the larynx, atony of certain muscles, or abductor paralysis. But it must be admitted that it is often difficult to differentiate between these various pathological conditions of the larynx, or to explain satisfactorily the exact cause of the difficulty.

Some writers believe that the conditions rendering the prolonged use of the tube necessary are rare, or even extremely infrequent. We have met with very many cases in which it was necessary to continue the use of the tube longer than the usual period of five or six days without development of the pathological changes which lead to chronic stenosis. Such cases are able to get along without the tube

in the course of two weeks, or three, at the longest. But postdiphtheritic stenosis occurs, according to our experience, in from 1 to 3 per cent. of all cases of intubation. Dillon Brown is reported as saying that he has encountered it in the proportion of about once in 75 or 100 cases.

In discussing the causes of prolonged intubation but little consideration need be given to traumatism resulting from the introduction or removal of the tube. While it is true that the unskilful use of the introducer or extractor, or too much pulling upon the epiglottis during the operation, may cause abrasions and oedema of the soft parts, and thus make reintubation necessary, yet it is certain that the principal cause of "retained tubes" is not due to such an injury, but to traumatism in the larynx occasioned by the tube itself. It is important that the tube should properly fit the larynx; it certainly should not be too large. But no matter how well it fits, it sometimes causes ulceration. It should, therefore, be

dispensed with as soon as possible. It, however, should not be removed until there is reason to believe the patient can get along without it; for removing it too early would necessitate its reintroduction, and thus the risk of traumatism would be increased.

When the tube is required longer than the usual length of time on account of the persistence of false membrane in the larynx, the condition, from our present point of view, is not serious, for as soon as the membrane disappears the tube can be dispensed with.

We believe that the most common cause for retention of the tube, at least primarily, is subglottic laryngitis with oedema. Later, as the tube is worn longer, and has been removed and reintroduced many times, tissue changes of a destructive character sometimes take place in the larynx, with a marked tendency to terminate in chronic stenosis. We have removed, *post-mortem*, larynges which showed considerable loss of tissue from ulcerative action. These ulcers heal by granulation and the formation of cicatricial tissue, and hence permanent stenosis to a greater or less degree is liable to result in such cases.

Many of the cases with subglottic laryngitis and oedema improve after two or three intubations, and recovery follows without any untoward symptoms. Other cases are more troublesome, especially those which develop also atony of the muscles or abductor paralysis. With

Fig. 109



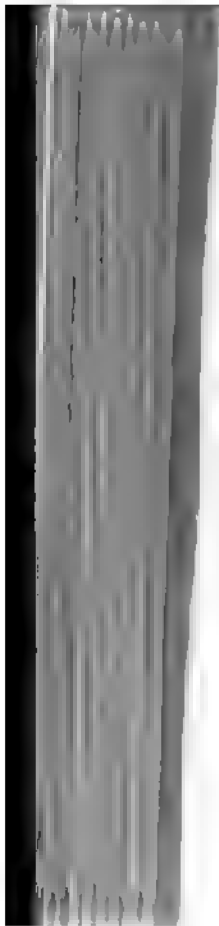
Pressure ulcer due to intubation. (Zaginsky.)

PLATE LIX.



Larynx and Trachea Removed at Autopsy.

Showing a large roundish ulcer caused by pressure of the intubation tube. The lower linear wound was the result of a tracheotomy. From a patient in the Municipal Hospital. (Photographed by Dr. E. N. Fought.)



this complication it may be necessary to repeat intubation many times, and the patient is fortunate if he escapes ulceration of the larynx. He, however, rarely escapes bronchopneumonia, more or less marked.

When there is marked ulceration of any part of the larynx, with little or no œdema, the child may get along fairly well without the tube for a few days, but as cicatrization takes place the lumen of the larynx becomes gradually diminished, with a corresponding increase of dyspnoea. In attempting to perform intubation in such a case, it has been found impossible to introduce the tube. We have been confronted with this difficulty more than once, and in order to save the child's life have resorted to tracheotomy.

In cases of ulceration of the larynx we believe it is good practice to use the tube intermittingly until the ulcers have cicatrized. If there is difficulty in introducing the tube it had better be left undisturbed for a long time—*i. e.*, from one to two weeks at least. In cicatricial stenosis, however, after the difficulty is overcome of introducing a tube, though small, but of sufficient calibre to supply the lungs with air, it is comparatively easy, after this tube has been worn for a day or two, to introduce a larger one. Having thus restored the normal lumen of the larynx, it is advisable to insert the tube two or three times a week for a while, leaving it in place from twelve to twenty-four hours. Later, as the conditions improve, it need not be introduced so frequently. But the tube should not be dispensed with until the tendency to recontraction of the cicatricial tissue has been overcome.

In cases of prolonged intubation the vulcanite tube should by all means be preferred. The calcareous deposits which always form on metallic tubes make them very objectionable. They cannot be worn long without causing irritation and often ulceration of the larynx. As these deposits do not form on hard-rubber tubes, they may be allowed to remain in position for a long time without doing harm. One of our cases of four years' standing has worn a vulcanite tube continuously for periods of three months each, and once as long as five months without removal, with no unpleasant consequence except, as the parents say, an offensive breath. The tube never showed any calcareous deposits. It is worthy of remark that when the tube has been worn for a long time the child acquires the ability to swallow with little or no difficulty.

We have called attention to the fact that in some cases of prolonged intubation, after the tube has been removed for a few days, it is impossible to reintroduce it, and that *tracheotomy* becomes necessary. Likewise, this operation may be deemed expedient when the tube cannot be retained in position. We have seen cases in which the tube was constantly coughed up, even when it was two or three sizes too large. In such a case it sometimes happens that the head of the tube enters the postnasal space and suffocation threatens if the tube be not immediately removed or pushed down into the larynx. To keep it in place would require a constant attendant. Under such circumstances it is better to perform tracheotomy.

In this troublesome class of cases we are, however, reluctant to recommend tracheotomy except as a *dernier ressort*. This is because of the difficulty we have many times experienced in getting rid of a retained tracheal cannula. One such patient is at the date of writing in the hospital, having worn the cannula for about two months.

After returning to their homes, three of our patients of this description were taken to a general hospital in this city and placed under the care of a surgeon. An operation was performed with the view of overcoming the stenosis due to contraction of the cicatricial tissue in the larynx, but in each instance the operation was unsuccessful, and the tracheal cannula had to be continued. Two of these unfortunate children subsequently contracted pneumonia and died. There are three other ex-patients of whom we have knowledge with retained tracheal tubes; in one the retention, at the time of writing, has extended over a period of six months, and in the other two of about four years each.

The difficulty in getting rid of the tracheal cannula in this class of cases may not be due alone to cicatricial tissue in the larynx caused by the intubation tube. In addition to this a later obstruction is not infrequently developed as the direct result of the inflammation caused by the long-retained cannula. This occurs at the upper angle of the wound and may be in the nature of a stricture, or the larynx may be completely occluded by cicatricial tissue. This condition is even of more serious import than the former. We have seen two such cases in which it was impossible to pass a probe through the lumen of the larynx, either by way of the mouth or the tracheal wound; and the voice, even in the faintest whisper, was lost, which proved that no air passed through the larynx. According to O'Dwyer, a stricture of this description develops in a large proportion of young subjects when the operation is high, involving the cricoid cartilage or its immediate vicinity. He says: "When the wound is still higher, that is, wholly within the larynx, complete occlusion with adhesion of the vocal cords is very liable to occur," etc.

As to the treatment of chronic stenosis of the larynx, we believe that long-continued intubation offers the best results. As soon as the tube is once introduced, no matter how small it may be, the chief difficulty is overcome. After this, tubes of graduated sizes should be employed, one after the other, until the one suited to the age of the child is reached. As already stated, the tube may have to be worn intermittingly for a very long time before the cicatricial tissue loses its power to contract. The physician should not become discouraged too soon, but persevere, as it may sometimes require years to remedy the difficulty.

When occlusion of the larynx is complete, or nearly so, whether caused by the intubation tube or a long-retained tracheal cannula, it will be found impossible to introduce a croup tube of the smallest size. Such cases are difficult of management by the general practitioner and had better be referred to the laryngologist. We believe, however, that instead of attempting to force an entrance from above downward, it is better to etherize the patient and enlarge the tracheal wound at

its upper angle so as to admit of the introduction of a sound from below. In this way the sound is less liable to injure the parts by catching in the ventricles. The intubation tube should then be introduced and worn continuously for one or two weeks, after which it should be employed intermittently until a cure is effected. This procedure was recommended by O'Dwyer in a paper read before the British Medical Association in 1894, on "Treatment of Chronic Stenosis of the Larynx by Intubation." In this paper O'Dwyer says: "The length of time that intermittent intubation will be required to effect a permanent cure will be influenced largely by the amount of cicatricial tissue present, and its location. If confined to the chink a more speedy result may be expected, because of the stretching which is exerted by the expansion of the glottis with every breath. After the normal lumen of the larynx has been restored, or at least ample breathing room secured, a tube should be inserted once or twice a week, and allowed to remain in position from twelve to twenty-four hours. This interval can be gradually increased according to indications, and continued until the tendency to recontraction has been permanently overcome."

After the introduction of the intubation tube in these cases of chronic stenosis in which tracheotomy has been performed, it is desirable that the tracheal wound should be kept open for some time. If it could be kept patulous—a thing difficult to accomplish in a child—the liability of the tube being coughed out would be greatly lessened. A special tube or combination of tubes that would meet this indication seems to be an important desideratum. At any rate, O'Dwyer's advice should be heeded. It is as follows: "In practising intubation for the removal of a tracheal cannula, the wound under all circumstances must be kept open until sufficient breathing room through the natural passage has been secured to sustain life, in case the tube should be coughed out. This is, as a rule, extremely difficult to accomplish, especially in children. The hard-rubber plug devised by Drs. Pitts and Brook, and used in a series of cases, appears to be most practicable for this purpose. It is provided with a collar similar to that on a tracheal cannula, by which it can be held in position."

Shurly,¹ of Detroit, believes that the cure in cases of prolonged intubation may be hastened by smearing the tube with an ointment composed of alum and vaselin. Louis Fischer, of New York, likewise recommends 10 per cent. alum or ichthyol-gelatin.

¹ A paper read in the Section on Diseases of Children, American Medical Association, 1903, on "Prolonged Intubation Tubes, with a Method Leading to their Extraction."

CHAPTER XIV.

DIPHTHERIA (*Continued*).

THE SERUM TREATMENT OF DIPHTHERIA.

THE antitoxin method of treating infectious diseases may be said to have had its origin in the scientific investigations of Pasteur in 1880. He then made the discovery that an unusually mild attack of fowl cholera may be produced in chickens by inoculating them with an attenuated or non-virulent virus of that disease. Chickens thus inoculated, he found, were thereby rendered immune to this affection. He also applied this discovery to anthrax in sheep with similar results. Later—in 1886—Salmon and Smith showed the great practical value of Pasteur's discovery by an application of this principle to the protection of swine against hog cholera.

With a knowledge of the fact that the rat and the frog were peculiarly refractory to the operations of the anthrax bacilli, Behring showed by experiment that the blood taken from these animals was, within certain limits, efficacious against the production of anthrax in other animals.

In 1890 Behring and Kitasato startled the medical world with the announcement that if an animal be immunized against tetanus or diphtheria the serum of the blood of that animal, when injected in sufficient quantity, is capable not only of immunizing other animals against an attack, but also of effecting a cure when attacked. These observers published their discovery in the following language: "Our researches on diphtheria (Behring) and on tetanus (Kitasato) have led us to the question of immunity and cure of these two diseases, and we have succeeded in curing infected animals and in immunizing healthy animals, so that they have become incapable of contracting diphtheria or tetanus."

In this connection it is due Aronson to state that, with equal diligence in this field of labor, he also succeeded soon afterward in immunizing animals against diphtheria.

After the investigations of these men, it is only fair to mention the confirmatory experiments of Fraenkel, Wernicke, Roux, and others, who likewise succeeded in producing in animals an immunity against diphtheria by inoculating them with virulent or somewhat attenuated cultures or with diphtheria toxin. But, as already shown, Behring carried these researches one step farther by demonstrating that the blood of immune animals contained a substance which antagonizes

¹ Quoted by Lennox Browne, *Diphtheria and its Associates*

the diphtheria toxin. These important studies constitute the foundation upon which has been based the modern antitoxin treatment of diphtheria.

The last link in the chain of these interesting investigations having been forged, it now remained to apply the discoveries that had been made to their special purpose of curing diphtheria in human beings. Here, as in the entire field of this research, the work of Behring was most productive. He succeeded in reaching the goal of his investigations, and, together with Kossel, in 1893, recorded 30 cases of diphtheria in human subjects which had been benefited by the use of serum from the blood of animals artificially immunized.

In 1894, Ehrlich, Kossel, and Wassermann reported 223 cases treated with antitoxic serum, with a mortality rate of 23 per cent.

In June, 1894, Katz, a collaborer of Baginsky, reported to the Berlin Medical Society 128 cases of diphtheria which had been treated with serum produced from one of Aronson's horses. This number was subsequently increased by Baginsky to 163 cases, with the surprisingly low death rate of 12.9 per cent.

While the announcements of the foregoing results were received with intense interest, the culminating point of enthusiasm was reached at the Eighth International Congress of Hygiene and Demography, held at Budapest in September, 1894, when Roux presented his brilliant paper on the subject of the serum treatment of diphtheria (Lennox Browne). He announced that he had confirmed, by experiments in the Pasteur Institute, all the important statements made by Behring and others who labored contemporaneously, and presented the records of a large number of cases in which the serum treatment had been employed successfully in the human subject, "and," as Lennox Browne so aptly says, "by comparative statistics, enforced the attention of the whole medical world to a consideration of its claims."

Theory of the Action of Antitoxin.—There seems to be very little known as to the *modus operandi* of antitoxin in the treatment of diphtheria. It exerts no bactericidal effect upon the Klebs-Loeffler bacilli, although it is supposed to arrest the inflammatory process caused by these organisms. It is also believed that it does not act chemically or otherwise upon the toxin circulating in the blood, but rather upon the living cells of the body, through whose agency the cure is effected. Park says: "After the cells have been to a certain extent affected by the toxin, the protective power of the antitoxin can no longer be exerted and the lesions progress in spite of it."

While the mode of action of the antitoxic serum cannot be satisfactorily explained, yet there is no doubt that it is capable of neutralizing the effect of the toxin of diphtheria in animals. This has been demonstrated thousands of times in the laboratory by bacteriologists. Park says: "We have every reason to expect that, since the toxin in human diphtheria is, so far as we can determine, exactly the same toxin as that in diphtheria in animals, this power of the antitoxin to make harmless the toxin will manifest itself in man under similar conditions."

Preparation of Antitoxin.—As already pointed out, to render an animal immune to the diphtherial poison it is held to be sufficient to gradually accustom that animal to the action of the poison. The serum of an animal thus treated is believed to possess not only prophylactic but also curative qualities. The goat has been used in this way for the production of antitoxin; but in order to obtain a more abundant yield—as well as for some other reasons—the horse is the animal now generally preferred.

Having eliminated the possibility of the existence of glanders and tuberculosis by the proper tests, the horse is brought into a good condition by rest, diligent grooming, and careful feeding, preparatory to beginning the process of immunization. According to Park, the following method is employed in the production of antitoxic serum by the Health Department of New York City:

To prepare a strong diphtheria toxin a virulent culture of the Klebs-Loeffler bacillus, grown under special conditions, is, at the end of a week's growth, rendered sterile by the addition of 10 per cent. of a 5 per cent. solution of carbolic acid. In twenty-four hours it is filtered through sterile filter paper and stored in bottles in a cool place. A number of horses are injected with an amount of toxin sufficient to kill ten thousand guinea-pigs of 250 grams weight each (about 44 c.c. of strong toxin). With each injection of toxin 10,000 units of antitoxin are given. After from three to five days, when the fever has subsided, a second injection of a slightly larger dose is given. Increasing doses of toxin are then given at intervals of five to ten days, until, at the end of two months, from ten to twenty times the original amount is given. The horses are then bled and the blood serum tested for antitoxin. Those animals yielding less than 200 units in each cubic centimetre are discarded.

The remaining horses are then further treated with ascending doses of toxin. At the end of three months the serum should contain from 300 to 800 units of antitoxin to each cubic centimetre. The best horses will furnish high-grade antitoxin for years. A three months' freedom from toxin injection should be given the horses each year.

The blood is obtained by plunging a sharp-pointed cannula into the jugular vein. It is received in Ehrlenmeyer flasks and allowed to clot, the serum then being siphoned off.

Antitoxin is a proteid substance of unknown chemical composition. It is destroyed by heat 55° C., and is precipitated from its solution in the same manner as globulins.

As already pointed out, antitoxin possesses the property of neutralizing, within certain limitations, the diphtheria toxin within the body. That is to say, when a given amount of antitoxin is injected into an animal with or just before a certain quantity of the toxin, it abrogates the poisonous effect of the latter.

Behring and Ehrlich applied the term "antitoxin unit" to an amount of antitoxin capable of protecting the life of a guinea-pig weighing 250 grams from one hundred fatal doses of toxin. Ehrlich later

pointed out the variability of the diphtheria toxin, and therefore the liability of error in such standardization. Park, who experimented with toxins of different potencies, gives the following definition of an antitoxin unit: "The amount of antitoxin necessary to protect the life of a guinea-pig from one hundred fatal doses of a toxin similar to that adopted as a standard, namely, one having the characteristics of toxins in cultures at the height of their toxicity." He says: "This amount of poison is produced by the growth for one week of a virulent bacillus in 1 c.c. of bouillon."

The Serum.—The serum varies considerably in color, though it should be clear and free from anything that looks like bacterial growth. It is maintained in an aseptic state by putting it into sterilized bottles, which are hermetically sealed and kept in a cool place. It is quite common to use some preservative, such as camphor, carbolic acid, trikresol, and the like.

The serum on the market varies greatly in antitoxin units. It is believed that each cubic centimetre should contain at least 100 antitoxin units, but it is desirable to have it much stronger. Originally, Behring's firm put up three strengths in vials of about 10 c.c. each, as follows:

No. 1, containing 600 units, which was regarded as a suitable dose for a child at the onset of an ordinary attack of diphtheria.

No. 2, containing 1000 units, for a severe attack in children.

No. 3, containing 1500 units, for adults, or a very severe form of the disease in children.

The serum prepared in this country is put up in vials containing from 5 c.c. to 10 c.c., and represents a strength of 100 to 500 antitoxin units to each cubic centimetre. The number of units in each vial should appear on the label.

Dosage.—In considering the dose one should think of antitoxin units rather than the quantity of the serum; but it must be admitted that there is no fixed dose. In the present state of our knowledge it is impossible to fix the dose on the basis of age, as in the case of drugs. Perhaps most practitioners inject as many antitoxin units into a child as into an adult. This does not seem unreasonable when we consider that the amount of toxin absorbed, and which we seek to neutralize or counteract, is in all probability as great in the former as in the latter. It is also not improbable that the younger the child the greater the susceptibility to the toxin of the disease, with a less power of resistance, and "consequently," as Lennox Browne remarks, "if, as has been suggested, the remedy acts by cell stimulation, the greater the necessity for a large dose of the serum; or, in other words, since the young cell elements are so extremely sensitive to the diphtherial poison, they require to be fortified all the more strongly in order to exercise an effective resistance." We may state, on the authority of the writer just quoted, that Roux, in his first announcement, speaking of the serum prepared at the Pasteur Institute, advised that 20 c.c. (representing, probably, 2000 units) be given to every patient—adult, or child

above one year—so soon as seen, and even in advance of the bacteriological diagnosis, stating that for children under one year the first dose should be as many cubic centimetres as the child is months old. In very severe cases, he said, the dose should be as much as 30 c.c., or even more.

It has been deemed advisable by the most competent observers to regulate the dose according to the time that has elapsed since the onset of the disease and the severity of the attack. As we have just shown, Behring believed that a dose of 600 units was sufficient for a child at the onset of an ordinary attack, but if the case be very severe, or far advanced when first seen, the dose should be increased to 1500 units.

We feel that what Park¹ has said on the subject of dosage is worth quoting. He writes: "The size of the dose should be measured chiefly by the extent and intensity of the disorder; also, but to a less degree, by the size of the patient and the duration of the illness. For young children, with but moderate lesions of the tonsils or palate, a single dose of 1000 to 1500 units will suffice. For older children and adults 1000 to 2000 units should be given. In children who are already seriously ill or who already show the toxic effects, or in whom the larynx is involved, a dose of 1500 to 3000 units . . . is necessary.

"If the symptoms do not abate, another 1000 to 2000 units may be given on the following day. In a few cases still a third injection is required. Exceptionally, a week or ten days after administering the antitoxin, a slight return of exudate may appear; here another moderate injection is indicated. Where these doses have not benefited it is doubtful if larger ones will succeed.

"At the New York Hospital for Contagious Diseases for several months one-half of the severe cases received on admission 3000 units, and again on the following day 3000 more. If no improvement followed, a third 3000 units were given. The other half received 2000 units on admission, and a second 2000 in eighteen hours. So far as one could judge, those receiving the lesser amount did as well as those receiving the very large amounts. On the other hand, no additional disagreeable effects were noticed from the larger quantities."²

McCollom,³ of the South Department Hospital, Boston, recommends that antitoxin be administered in large doses. He advises that 4000 units be given at once, and that this dose be repeated at intervals of

¹ Loomis-Thompson, *American System of Practical Medicine*.

² While these pages are going through the press we note in the *Archives of Pediatrics*, December, 1904, an abstract of a discussion in the New York Academy of Medicine on the dosage of diphtheria antitoxin in which Dr. Park's views are given as follows: He said that for three years he had experimented with antitoxin in doses greatly varying in size; during one year the dose was 10,000 to 20,000 units, the next year it was between 5000 and 10,000 units; the third year it was between 3000 and 5000 units. He said it was very difficult to find out which dosage produced the best results.

In bad cases of diphtheria Dr. Park advocated using large doses. In mild cases, either early or late involving tonsils and pharynx, he used 2000 units. In severe early cases 4000 units; in ordinary laryngeal cases 5000 units. In malignant cases, tonsillar, pharyngeal, or nasal, 10,000 units, and repeating this dose at the end of twelve hours unless the patient is distinctly better. He emphasized the fact that the antitoxin should be given for the diphtheria and not for any accompanying condition like pneumonia.

³ A Plea for Larger Doses of Antitoxin, *Medical and Surgical Reports of the Boston City Hospital*, 1900, eleventh series.

twelve hours, presumably until improvement takes place. He says that since larger doses have been given the death rate among his cases of diphtheria has been materially reduced, the reduction being especially noticeable among the apparently moribund cases. The most satisfactory results were obtained when the serum treatment was begun at an early stage of the disease.

The dose employed by us in the Municipal Hospital, Philadelphia, has varied greatly. In our early experience with the remedy we followed the recommendations of Behring as to dosage. Finding, however, that the results were not as satisfactory as we were led to believe they should be, the dose was increased. For a few years we gave 1000 to 2000 units at a dose, which was repeated in severe cases at intervals of twelve hours, until two, three, or more doses were given. Later, the dose was considerably increased. For some months in succession, on one or two occasions, each patient admitted to the hospital received from 6000 to 9000 units, and this dose was repeated two or three times in many instances. We have more than once administered to a child 20,000 units at a single injection. Very many of our patients have received as much as 20,000 units, and even more, in divided doses. The largest total quantity which we have administered was 47,000 units to an adult female. This was given, of course, in divided doses. We are able to bear testimony with others to the fact that large doses of antitoxin do not appear to be harmful. Our experience is, furthermore, in accordance with Park's, in that we have found that the patients who received the medium-sized doses did as well as those receiving the extraordinarily large doses.

It appears preferable that the first dose should be a fairly large one—at least from 2000 to 4000 units. In very severe cases doses of 3000 units each should be repeated at intervals of twelve hours until 6000 to 12,000 units have been given. It is doubtful whether larger doses will afford any additional benefit.

All observers agree that antitoxin is most efficacious when administered promptly at the beginning of an attack of diphtheria. Some believe that it is useless after the third day of the disease. But if it should happen in any case that the disease is not recognized until a later stage, it is advisable to administer the remedy, and thus give the patient the benefit of the doubt.

It is our practice to administer antitoxin to all patients who are sent to the hospital with the diagnosis of diphtheria. This is a rule which is carried out irrespective of the stage of the disease or the result of the bacteriological examination. Immediately after admission a bath is given, and this is followed by a large dose of antitoxin, which is repeated in twelve to eighteen hours in the severer cases. The number of repetitions may depend upon the disposition of the membrane to separate and peel off.

The Effect of Antitoxin upon the Local Process.—According to Roux and most other writers the effect of antitoxin upon the pseudomembrane of diphtheria is very prompt and positive. Many observers have found

that the membrane ceased to spread in twenty-four hours after the dose was given, commenced to separate twenty-four hours later, and entirely disappeared in the course of four or five days, leaving the mucous membrane of the fauces quite normal. It has been frequently noted that the false membrane early undergoes a whitening process, with fissuring of its surface, causing it to resemble, in the imagination of some writers, "chicken fat." It is believed that the underlying tissue is less liable to be destroyed by ulcerative action, and that the membrane may often be detached and removed with but little or no hemorrhage. Recurrence of the membrane is believed to be less frequent than under the old treatment.

Antitoxin, according to some observers, also exerts a favorable influence upon the constitutional symptoms. It is often mentioned in clinical reports that the temperature begins to fall and general improvement takes place as soon as the serum is injected. We have called attention to the fact that the temperature in diphtheria is not high, except at the onset of the disease. It usually falls to normal, or nearly so, on the third or fourth day of the illness. A persistently high temperature would indicate the presence of some complication.

Mode of Administering Antitoxin.—Any syringe capable of being sterilized, and large enough to hold 5 to 10 c.c., may be used to inject the serum. It matters but little where it is injected. Some prefer one place, and others another. We usually select the lower abdominal region, for the reason that any local tenderness following the injection is not aggravated by the pressure of clothing, or by the patient's recumbent position. The syringe having been sterilized by means of boiling water, the skin at the site selected should be thoroughly scrubbed with soap and water and then washed with alcohol. After filling the syringe with the antitoxin it should be held with the point upward and the piston pushed in slightly so as to exclude the bubbles of air. The skin is then pinched up by the thumb and forefinger of one hand, the needle introduced, and the serum injected slowly. After withdrawing the needle a pad of cotton-wool may be placed over the site of puncture, and this with the exuding drop of serum seals the wound similar to collodion. The material is readily absorbed. For about twenty-four hours after the injection has been given, there is usually a localized redness, with slight edema, and moderate pain on pressure. Abscesses sometimes occur; but they are rare when the technique is faultless.

Limitations of Antitoxin.—It is not claimed for diphtheria antitoxin that it exerts any neutralizing influence over the poison elaborated by the bacteria commonly associated with the Klebs-Loeffler bacilli. In considering the symptomatology of diphtheria we called attention to the fact that this affection is not infrequently a complex disease, and that dangerous symptoms are sometimes produced by the toxins of the associated organisms. It is evident that the influence of antitoxin in such cases must be limited.

Park says: "Another limitation is suggested by the results of experiments upon animals. It is known that after the infection has proceeded

to a moderate degree it cannot be arrested by antitoxin. Experience shows that in human beings also the cells no longer react to antitoxin after a certain degree of poisoning has taken place, and this point in some cases seems to occur very early. I doubt if we are justified in saying that in these the actual lesions have progressed so far that without any further poisoning life has become impossible. I believe it may be possible that even after the administration of antitoxin the poison goes on producing further lesions, the cells already affected by the toxin not responding to the antitoxin. There are exceptional cases in which even when the antitoxin is given early it apparently fails to fortify the cells against the diphtheria poison."

The Prophylactic Power of Antitoxin.—It has been shown by many observers that antitoxin injected subcutaneously will protect an individual against an attack of diphtheria. Immunity thus conferred, however, does not last very long—only about two or three weeks. But protection may be continued by a repetition of the injection. For immunizing purposes small doses have been found to be sufficient (300 to 500 units, according to the age and size of the person).

Jacobi cites Slawyk's report¹ as showing the prophylactic power of diphtheria antitoxin. It appears that in Heubner's division of the Charité Hospital of Berlin relapses of endemic outbreaks were quite common in spite of careful preventive measures until immunization by antitoxin was resorted to. The dose administered was 200 units, repeated every three weeks. In this way the place remained free from the disease. As a matter of experiment immunization was discontinued for one month, when three cases of diphtheria occurred, one of which terminated fatally. The preventive injections were then renewed, and during the following two and a half months, up to the time the report was published, no new case had occurred.

Similar results have been observed in New York and elsewhere. Park has shown that the work done along this line by the New York Health Department has been very successful. Many children of families in which diphtheria occurred were protected against the disease by immunizing doses of antitoxin. Most of these instances were among the tenement-house population. The cases detailed number altogether 1043. He says: "In a large percentage of the whole number diphtheria bacilli were present in the throat when the serum was administered, and all had been exposed to diphtheria under conditions more or less favorable for the transmission of the disease. Among those immunized 3 cases of diphtheria occurred between one and thirty days after the treatment—*i. e.*, 1 on the twelfth, 1 on the seventeenth, and 1 on the nineteenth day, respectively." He also says that by the use of this agent it has been possible to stamp out diphtheria in four large institutions for the care of children in which it was prevailing in more or less epidemic form.

Park² has summarized the 1043 cases as follows:

¹ Deutsche medicinische Wochenschrift, 1898, No. 6.

² Loomis-Thompson, American System of Practical Medicine.

	No. of cases immunized.	No. of units of antitoxin administered.	No. of cases of diphtheria developing among those immunized between one and thirty days.	No. of cases developing within twenty-four hours.	No. of cases of diphtheria developing after thirty days.	No. of cases of diphtheria that occurred in the institution previous to immunization.
New York Infant Asylum (first immunization).	224	100 to 200	1 mild on 19th day.	0	6	107 cases in 105 days.
New York Infant Asylum (second immunization).	245	125 to 225	1 mild on 12th day.	0	4	6 cases in 12 days.
Nursery and Child's Hospital.	136	50 to 200	0	0	0	45 cases in 30 days 15 cases in 15 days.
New York Juvenile Asylum.	81	150 to 250	0	0	0	12 cases. 2 cases in 2 days.
New York Catholic Protectory.	114	150 to 500	0	1	0	5 cases in 3 days.
Bellevue Hospital.	11	175 to 225	0	0	0	2 cases in 10 days.
Health Department, Inspectors.	232	150 to 250	1 mild on 19th day.	3	{ 1: 80 { 1: 31 { 1: 55	1 or more cases to more than 94 families.
Total.	1043	3	4	13	

Zuppinger,⁴ in reviewing the experience of others in various countries on the preventive serum treatment against diphtheria, presents his own. He says that out of 1000 children exposed to this malady and treated by preventive injections of antitoxin, only 18 developed the disease later. Of this number, he believes that 11 had already contracted diphtheria, as the symptoms developed at once. This leaves only 7 cases in which the antitoxin failed to protect.

The Commissioner of Health of Chicago says that out of 7051 exposed persons who received each an immunizing dose of antitoxin (500 units), only 46 subsequently developed diphtheria, but all recovered.

In the Municipal Hospital, Philadelphia, we have frequent opportunities of noting the immunizing power of antitoxin. Each year many patients are sent to the hospital as subjects of diphtheria when the disease turns out to be something else. They occupy the diphtheria wards, and consequently are freely exposed to the infection of that disease. As these patients are supposed to be suffering from diphtheria the resident physician injects the antitoxin as soon as possible after admission. The dose administered may be from 3000 to 6000 units. We have no record of any such patient falling ill with diphtheria while in the hospital. For the last three years we are able to report 193 observations of this kind.

Evidence of the Curative Power of Antitoxin. While it is believed that all forms of diphtheria are liable to be benefited by antitoxin, the greatest benefit is to be expected and doubtless does result among

⁴Preventive Antitoxin Treatment, Wiener klinische Wochenschrift, Vienna.

the uncomplicated cases, or those not suffering from a mixed infection. The mortality rates, therefore, will be found to vary, accordingly as the complex cases are included or excluded in the compilation of statistics.

Since the advent of antitoxin, diphtheria statistics, both of hospitals and of private practice, have greatly increased and are constantly growing. After carefully reviewing this large amount of published data, Biggs and Guerard arrived at the following conclusions:¹ "It matters not from what point of view the subject is regarded if the evidence now at hand is properly weighed, but one conclusion is or can be reached—whether we consider the percentages of mortality from diphtheria and croup in cities as a whole, or in hospitals, or in private practice; or whether we take the absolute mortality for all the cities of Germany whose population is over 15,000, and all the cities of France whose population is over 20,000; or the absolute mortality for New York City, or for the great hospitals in France, Germany, and Austria; or whether we consider only the most fatal cases of diphtheria, the laryngeal and operative cases; or whether we study the question with relation to the day of the disease on which treatment is commenced, or the age of the patient treated; it matters not how the subject is regarded or how it is turned for the purpose of comparison with previous results, the conclusion reached is always the same, namely, there has been an average reduction of mortality from the use of antitoxin in the treatment of diphtheria of not less than 50 per cent., and under most favorable conditions a reduction to one-quarter, or even less, of the previous death rate. This has occurred not in one city at one particular time, but in many cities, in different countries, at different seasons of the year, and always in conjunction with the introduction of antitoxin serum and proportionate to the extent of its use."

Among the earlier effects of antitoxin is the whitening process which the false membrane undergoes. Following this, the membrane begins to separate, and, according to Roux and many other observers, entirely disappears in four or five days after the injection of the serum.

The subjoined table shows the day of the disease when antitoxin was administered to 350 patients in the Municipal Hospital, Philadelphia, and the day on which the throat was declared free of membrane. These were not selected cases, but taken at random.

¹ Quoted by Park, *Twentieth Century Practice of Medicine*.

**THE DAY OF THE DISEASE ON WHICH THE THROAT WAS DECLARED
FREE OF MEMBRANE.**

Day of disease on which anti- toxin was administered	No. of cases.	1st	2d	3d	4th	5th	6th	7th	8th	9th	10th	11th	12th	13th	14th	15th	16th	17th	18th	19th	20th	21st	
First	25	..	1	2	3	6	5	3	2	2	..	1											
Second	118				8	17	19	18	12	10	10	13	4	2	1	3			1	On the 23d. case.
Third	91					6	16	16	15	10	9	7	2	2	..	3	1		1	2	1		
Fourth	58						1	7	8	7	10	5	3	3		1	4			1	2		
Fifth	26							2	3	3	6	2	1	1	1		1	1			
Sixth	12									2	3	1	1	1	2	..		1				On the 30th. case.	
Seventh	8										1	4	1	1								On the 27th. case.	
Eighth	12										4	2	2	..	1		1	..	2				
Ninth	4											1	1	1	1								
Tenth																							
Eleventh	1														1								
Total	350	..	1	2	11	29	41	46	45	35	42	35	15	10	8	7	6	1	5	3	3	1	

It may be seen in the above table that the earlier in the disease the antitoxin was administered, the sooner the membrane disappeared.

Lennox Browne, however, believes that antitoxin is not a very important factor in hastening the separation or disappearance of the membrane. He shows comparisons between 92 cases treated with serum and 67 without, as follows:

**DAY OF TREATMENT ON WHICH THE THROAT WAS DECLARED FREE OF
MEMBRANE.**

Day	Series A, without serum.	Series B, with serum
Second	4 cases or 6 per cent.	1 case or 1.08 per cent
Third	13 " 20 "	4 cases or 4.3 "
Fourth	14 " 21 "	9 " 9.8 "
Fifth	14 " 21 "	18 " 19.5 "
Sixth	8 " 12 "	18 " 19.5 "
Seventh	6 " 9 "	10 " 10.8 "
Eighth	5 " 7.4 "	2 " 2.1 "
Ninth	1 case or 1.5 "	1 case or 1.08 "
Tenth	1 " 1.5 "	1 " 1.08 "
Eleventh	1 " 1.5 "	0 " "
Twelfth	..	2 cases or 2.1 "
Thirteenth	..	2 " 2.1 "
Fourteenth	..	2 " 2.1 "
Seventeenth	..	1 case or 1.08 "
Twenty-fourth	..	1 " 1.08 "
Twenty-eighth	..	1 " 1.08 "
Thirty-ninth	..	1 " 1.08 "
	67	74 18 92

The author of this table says: "In Series A this fact (the day on which the membrane disappeared from the throat) was noted in only

67 of the cases, and in 92 in Series B. Only 1 occurred (in Series A) in which membrane reappeared, and that on the fourteenth day after admission; whereas, in Series B there were 5 cases of reappearance, 13 cases in which death occurred before it had cleared entirely, and in 1 case it was observed as late as the thirty-ninth day after admission, and the forty-first day of the disease."

Antitoxin in Laryngeal Diphtheria.—Many observers believe that antitoxin is more useful in laryngeal diphtheria than in any other variety. But, as faucial or nasal diphtheria is more frequently followed by toxæmia, it would seem that the serum treatment should be most efficacious in these forms of the disease. There is, however, no lack of evidence to prove that the mortality rate of membranous croup has been greatly lessened since the advent of antitoxin.

In 1893 von Ranke reported 1445 intubation cases of laryngeal diphtheria with a death rate of 62.5 per cent. Later, with antitoxin, he treated 342 similar cases with a reduced death rate of 28.9 per cent.

In Baginsky's service, in 1895, during a period of two months when the serum could not be obtained, there were 116 cases of laryngostenosis, with a death rate of 62.2 per cent.; while with the serum treatment, just before and immediately after this involuntary pause, the mortality was 37.8 per cent.

Kronlein (Zurich), in his report to the Twenty-seventh Congress of German Surgeons (1898), showed that previous to the use of antitoxin about one-half of all the croup cases observed in the clinical hospitals of the university had to be operated upon, but from the use of this agent the proportion has fallen to 23.1 per cent. While the average mortality among the operated (tracheotomy or intubation) cases was, formerly, 66.1 per cent., it has been reduced to 35.6 per cent.

The Committee of the American Pediatric Society on the "Collective Investigation of the Antitoxin Treatment of Laryngeal Diphtheria in Private Practice, 1896-97," arrived at the following conclusions: "First, that before the use of antitoxin it was estimated that 90 per cent. of laryngeal diphtheria cases required operation; whereas now, with the use of antitoxin, 39.21 per cent. require it. Second, that the percentage figures have been reversed; formerly 27 per cent. approximately representing the recoveries, while now, under antitoxin, 27 per cent. represents the mortality."

Dr. J. S. Billings, Jr.,¹ presents the following tabulation of cases of laryngeal diphtheria, operative and non-operative, treated in New York City with antitoxin by various physicians, from October 1, 1895, to January 1,¹1903:

¹ New York Medical Journal and Philadelphia Medical Journal, December 12, 1903.

	Laryngeal cases.			Non-operative cases.			Operative cases.		
	Cases.	Deaths.	Mortality per cent.	Cases.	Deaths.	Mortality per cent.	Cases.	Deaths.	Mortality per cent.
	2504	629	25.1	1843	389	21.1	661	246	37
Moribund cases deducted, . . . }	319	319	..	211	211	..	108	108	..
Remain . . .	2185	310	14.2	1632	178	10.9	553	132	23

Goodall, of London, published in the *British Medical Journal*, 1895, vol. i. p. 197, the following interesting statistics:

CASES OF LARYNGEAL DIPHTHERIA TRACHEOTOMIZED AND TREATED WITHOUT ANTITOXIN.

Authority.	Cases.	Recoveries.	Recovery per cent.
Sanné hôpital des enfants malades . . .	2351	690 ¹	29.3
Sanné (hôpital Sanné Eugène) . . .	2312	599 ²	25.6
E. Hirsch . . .	1654	517	31.2
Antitoxin Com. of Clinical Society . . .	1631	424	25.3
Asylum Boards Hospital, 1889-1893 . . .	323	104	32.1
" " " 1894 . . .	281	77	29.5
Clubbe (Sydney Children's Hospital) . . .	199	64	32.0
Guerant . . .	156	29	18.0
Eastern Hospital, 1892-1893 . . .	140	30	21.4
	8927	2543	28.4

CASES OF LARYNGEAL DIPHTHERIA TRACHEOTOMIZED AND TREATED WITH ANTITOXIN.

Authority	Cases.	Recoveries.	Recovery per cent
Asylum Boards Hospital	680	334	56.4
American Pediatric Society	668	446	72.7
Collected by Welch (W. H.) from 30 reports	515	313	60.4
Beaun, Strassburg . . .	132	88	66.6
Clubbe, Sydney . . .	129	80	62.0
Roux . . .	121	65	53.7
University College Hospital	72	63	73.6
Corné, Frankfurt . . .	54	37	68.4
	2374	1506	63.4

In the Willard Parker Hospital, New York, the mortality among the intubation cases of membranous croup continues high in spite of the antitoxin treatment. Through the courtesy of Dr. Louis Fischer, one of the attending physicians to the hospital, we are able to present the results for the years 1901-2-3, as follows:

Year.	Intubation cases.	Deaths.	Mortality per cent
1901 . . .	222	152	68.47
1902 . . .	258	142	55.04
1903 . . .	352	229	65.06
Total . . .	832	523	62.87

¹ Including 76 cases discharged uncured

² Including 90 cases discharged uncured

In the Municipal Hospital of Philadelphia the mortality rate among intubation cases of laryngeal diphtheria also continues high, as may be seen in the following table:

Year.		Intubation cases.	Deaths.	Mortality per ct.
1894.	Without antitoxin	100	75	75.0
1895.	About 50 per ct. of the cases received antitoxin	122 ¹	67	54.91
1896.	With antitoxin	156 ²	94	60.25
1897.	" "	182	127	69.78
1898.	" "	149	104	69.99
1899.	" "	165	97	58.78
1900.	" "	202	111	54.95
1901.	" "	139	66	47.47
1902.	" "	110	54	49.09
1903.	" "	110	55	50.0
		1435	850	59.23

The average rate of mortality among the above cases since anti-toxin has been employed is 58.05 per cent. There has been no deduction in either series in the case of patients admitted moribund or when believed to be beyond hope, as is the practice in some other hospitals.

Dr. J. H. McCollom, of the South Department Hospital, Boston, furnishes the following table showing the number of cases of laryngeal diphtheria treated by intubation in the Boston City Hospital, proper, and in the South Department, from 1888 to 1903, inclusive:

Preantitoxin Period.				Antitoxin Period.			
Year.	No. of intubation cases.	Deaths.	Per cent. of mortality.	Year.	No. of intubation cases.	Deaths.	Per cent. of mortality.
1888	100	78	78.00	1895	118	64	54.23
1889	128	104	81.25	1896	224	145	64.73
1890	93	79	84.94	1897	146	67	45.88
1891	50	42	84.00	1898	71	42	59.15
1892	65	56	86.15	1899	192	63	32.81
1893	109	90	82.56	1900	259	87	33.59
1894	89	74	83.14	1901	184	58	31.52
				1902	145	49	33.79
				1903	139	37	26.61
Total	634	523	82.49		1478	612	41.40

This table shows that the former death rate of 82.49 per cent. of laryngeal diphtheria treated by intubation in the above-named hospital has been reduced to 41.40 per cent. since the employment of antitoxin.

Results in Diphtheria (including Membranous Croup).—We have just referred to the results of antitoxin in laryngeal diphtheria, and will now speak of its results in diphtheria in general.

In 1897 Rauchfüss³ communicated to the Twelfth International Medical Congress, at Moscow, the most extensive statistics that have yet been collected on the subject of serum therapy in diphtheria. They give the results of the enquiry throughout the Empire

¹ Of those which received antitoxin the death rate was 52.94 per cent.
² Twenty-four of this number did not receive antitoxin.
³ Quoted by Bayeux, *La diphtherie*, Paris, 1899.

of Russia undertaken by the Pediatric Society, and the Society of Russian Physicians at St. Petersburg. The figures include 44,631 cases, all of which refer to positive cases of diphtheria. They were secured from fifty-one of the eighty-nine governments and districts of Russia, and are as follows:

Years.	Diphtheria treated without antitoxin.			Diphtheria treated with antitoxin.		
	Cases.	Deaths.	Per cent.	Cases.	Deaths.	Per cent.
1895	4521	1424	31.4	19,619	3163	16.1
1896	991	460	45.4	19,630	3694	18.6
1896-1897 . . .	996	335	33.5	5,892	675	12.5
Total	6507	2219	34.1	44,631	6522	14.6

We notice here a reduction from 34.1 per cent. to 14.6 per cent. by the serum treatment.

The following table shows the comparative mortality from diphtheria in the Russian hospitals before and since the advent of serum therapy. The figures are based upon the official report of Dr. S. Ippolitow on Serotherapy in Russia:¹

DIPHTHERIA TREATED IN RUSSIAN HOSPITALS.

Years.	No. of cases.	Deaths.	Mortality per ct.
1887 (without antitoxin)	6,115	1,882	30.8
1888 " "	6,546	1,964	30.0
1889 " "	6,214	1,732	27.9
1890 " "	6,940	1,971	28.4
1891 " "	7,252	1,875	25.8
1892 " "	7,022	2,175	31.0
1893 " "	8,493	2,692	31.7
1894 " "	12,068	3,760	30.5
Total	60,651	17,804	29.38
1895 (with antitoxin)	18,116	3,550	19.6
1896 " "	16,638	2,438	14.5
Total	34,754	5,988	17.22

The above table shows that the average mortality before the serum treatment was 29.38 per cent.; since the serum treatment, 17.22 per cent.

We think it proper to state what Prof. Kassowitz, of Vienna, has said of the mortality from diphtheria in St. Petersburg. In a second paper on the diphtheria serum question, he reiterates his former views, and by means of charts and statistics endeavors to maintain his position that antitoxin is of little if any therapeutic value. He presents statistics which we tabulate, as follows:

¹ Medical Department of the Russian Ministry of the Interior

² Therapeutische Monatshefte, 1902, vol. xvi p. 499.

DIPHTHERIA MORTALITY IN ST. PETERSBURG.

Preantitoxin Period.			Antitoxin Period.		
Years.	Deaths.	Deaths in each 10,000 of population.	Years.	Deaths.	Deaths in each 10,000 of population.
1891 . . .	349	3.6	1895 . . .	807	8.5
1892 . . .	338	3.5	1896 . . .	1188	11.6
1893 . . .	378	3.9	1897 . . .	1949	20.5
1894 . . .	1027	10.8	1898 . . .	1356	12.0
			1899 . . .	1096	9.7
			1900 . . .	1134	10.0
			1901 . . .	1434	12.7
Average . .	522	5.4	Average . .	1272	12.1

Kassowitz says: "The diphtheria mortality that has maintained itself at so fearful a height, as in fact it has in St. Petersburg during the past seven years under the beneficent influence of the serum treatment, was exceptional even before the days of the serum application."

Kassowitz reproduces graphic charts from an article published by de Maurans,¹ in which it is shown that the mortality from diphtheria in Birmingham, Liverpool, Dublin, and Stockholm has strikingly risen during the serum period. The rise began in some instances a year or so before the use of serum and in others after its use.

This writer still further shows that the curves of diphtheria mortality were not influenced by the introduction of serum treatment in Budapest, Glasgow, Zurich, Lille, Cologne, Berne, Christiana, Berlin, Lyons, Brussels, Leipzig, Edinburgh, Paris, Geneva, Copenhagen, Havre, Nantes, Toulouse, Turin, Antwerp, Stuttgart, Munich, Hamburg, Buenos Ayres, and London.

As tending to show the inutility of antitoxin, Kassowitz says that in 1897, according to the German Imperial Board of Health Reports, 42.9 per cent. of those who died of diphtheria were given serum within three days of the onset of the disease, and 22 per cent. within two days.

The value of the antitoxin treatment is forcibly demonstrated in the reports of the Metropolitan Asylums' Board. In 1894, 3042 patients of all ages were treated without serum, in the hospitals controlled by the Board, with 902 deaths—a death rate of 29.6 per cent. In 1895, the first year of the serum treatment, 3529 patients were thus treated, with a death rate of 22.5 per cent. This shows a fall in the mortality of 7.1 per cent. In the annual report of the Metropolitan Asylums' Board for 1901, it appears that, in that year, 6499 cases of diphtheria were treated with antitoxin in the Board's hospitals, with 817 deaths—a death rate of 12.5 per cent. There has, therefore, been a reduction in the mortality from 29.6 per cent. in 1894, without antitoxin, to 12.5 per cent. in 1901, with antitoxin. The treatment in other respects is said to have been the same.

According to this report, the laryngeal cases treated in the Board's hospitals in 1901 with antitoxin numbered 753, of which number 159 died, yielding a death rate of only 21.1 per cent.

¹ *Semaine médicale*, 1901, p. 401.

Goodall,¹ of London, presents the following compilation of statistics from reports of the statistical committee of the Metropolitan Asylums' Board, showing the case mortality of the city of London, before and since the advent of antitoxin:

	Before antitoxin			Since antitoxin		
	1892	1893	1894	1895	1896	1897
Mortality per cent. of all notified cases	23.8	24.8	24.7	21.2	19.9	17.4
Mortality per cent. of notified cases admitted to } Asylums' Board hospitals }	24.8	27.1	25.0	18.3	17.7	14.1
Mortality per cent. of notified cases not admitted	21.5	23.7	24.5	23.3	21.3	20.1
Per cent. of notified cases admitted to hospitals	30.1	24.5	30.8	41.5	39.9	41.4

Goodall also shows the case mortality of diphtheria treated in the hospitals of the Metropolitan Asylums' Board, as follows:

TABLE I.

1892.	1893.	1894.	1895.	1896.	1897.
29.5	30.4	29.2	22.8	21.2	17.6

" Later years contain larger number of adults."

TABLE II.—Mortality in children under five years of age.

1892.	1893.	1894.	1895.	1896.	1897.
51.5	53.3	43.9	39.5	30.3	24.9

" Including fatalities from other diseases combined with or following diphtheria."

The annual reports on the work of the Metropolitan Asylums' Board for the year 1903 show that the Board received during the year notifications of 7582 cases of diphtheria, of these 7072 were treated in the hospitals, with a death rate of only 9.6 per cent. The average death rates in the Board's hospitals in quinquennial periods since the year 1887 are as follows:

1887 to 1891	1892 to 1896	1897 to 1901	1902 and 1903
33.6 per cent	27.5 per cent	13.7 per cent.	10.4 per cent

According to a pamphlet issued by the authorities of the Institute for Infectious Diseases, of Japan, the serum treatment of diphtheria has affected the statistics of this disease in that country as follows. Previous to the sale of serum the average death rate of diphtheria patients was 50 per cent., but since the sale began it has gradually decreased to 38 per cent. in 1896, 36 per cent. in 1897, and finally as low as 28 per cent. in 1902.²

Most of the statistics collected in this country are equally positive as showing the value of antitoxin in the treatment of diphtheria. The

¹ British Medical Journal 1899, vol. 1, p. 197.

² It is interesting to note in this pamphlet that while the death rate from diphtheria in Japan has been greatly reduced since the advent of antitoxin there has been a large increase of both cases and deaths annually.

comparative mortality from this disease in Chicago, before and after the introduction of the serum treatment, as shown in the *Bulletin* of February 13, 1904, of the Health Department of that city, is as follows: During the preantitoxin period the deaths annually per 10,000 of population were 12.45 per cent., while since the serum has been used the ratio of deaths has been reduced to 4.55 per cent. The increase of population amounts to 52 per cent.; the decrease of diphtheria deaths, 63.4 per cent. Between October 5, 1895 (date of first case treated) and December 31, 1903, the Health Department treated 7435 cases of bacterially verified diphtheria, of which number 479 died, yielding a death rate of 6.44 per cent. It is stated that the average mortality without antitoxin still remains about 35 per cent.

We are indebted to Dr. J. H. McCollom, of Boston, for the following table, showing the ratio of morbidity and of the mortality of diphtheria in Boston, per 10,000 of population, for ten years—1894 to 1903 inclusive:

Years.	Population.	Cases.	Ratio of morbidity.	Deaths.	Ratio of mortality.
1894	486,880	3019	61.01	878	18.03
1895	501,083	4059	81.00	654	11.73
1896	516,305	4489	86.94	572	9.80
1897	528,912	3398	64.24	456	7.77
1898	541,827	1661	30.65	185	3.15
1899	555,057	2836	51.08	304	4.99
1900	560,892	4977	88.73	537	9.57
1901	573,579 .	3319	57.86	353	6.15
1902	588,741	1940	34.72	225	3.82
1903	600,929	2091	34.79	211	3.51

McCollom says the South Department Hospital of Boston was opened for patients September, 1895, and antitoxin has been given to every case of diphtheria admitted. In 1896 he published the following table, which shows the number of patients, by ages, admitted to the hospital from September 1, 1895, to May, 1896, together with the mortality rate in each age period:

Age.	Cases.	Deaths.	Mortality per ct.
Under 1 year	17	3	17.64
1 to 2 years	74	20	27.02
2 " 3 "	136	37	27.2
3 " 5 "	329	55	16.71
5 " 10 "	410	39	9.51
10 " 20 "	189	9	4.76
20 years and upward	206	7	3.38
	1359	170	12.5

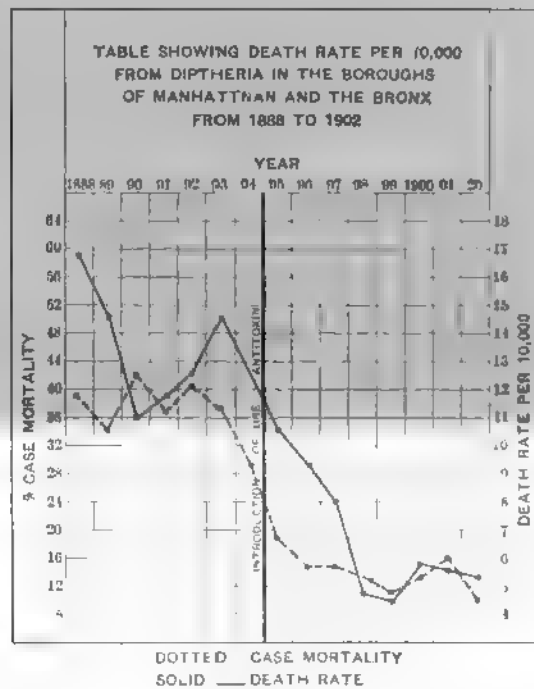
In presenting these statistics McCollom says that from February, 1891, until February, 1894, there were 1062 cases of diphtheria, with 493 deaths—a death rate of 46.42 per cent.

The cases treated in the South Department Hospital, Boston, since the introduction of antitoxin have yielded the following annual mortality:

DIPHTHERIA

Year.	Cases.	Deaths.	Mortality per ct.
1895	844	98	11.37
1896	1,779	276	15.54
1897	1,291	181	14.02
1898	892	108	11.54
1899	1,672	180	10.79
1900	2,000	294	11.2
1901	1,446	172	11.97
1902	1,018	108	10.11
Total	11,544	1405	12.17

In an interesting paper detailing the results of antitoxin in New York City in 1902, by Dr. J. S. Billings, Jr.,¹ the following diagram appears



This diagram shows in a very striking manner how greatly the mortality from diphtheria in New York City has diminished since the introduction of the serum treatment.

After presenting considerable statistical evidence, Billings concludes his paper by saying: "There is no longer any doubt as to the curative action of antitoxin in diphtheria. Of 15,792 cases injected with antitoxin furnished free of charge by the Department of Health or by its inspectors, 1860 died, a case fatality of 11.8 per cent. If the cases moribund when injected (722 in number) are deducted the case mortality is further reduced to 7.5 per cent."

¹ New York Medical Journal and Philadelphia Medical Journal December 12, 1903.

The statistics of the Willard Parker Hospital, however, show practically no reduction now over the preantitoxin period. We are indebted to Dr. Louis Fischer, one of the attending physicians to the hospital, for the data in the following table:

CASES OF DIPHTHERIA TREATED IN THE WILLARD PARKER HOSPITAL, NEW YORK CITY, FROM 1889 TO 1903.

Preantitoxin Period.					Antitoxin Period.				
Year.	Cases.	Deaths.	Mortality per cent.	Year.	Cases.	Deaths.	Mortality per cent.		
1889 . . .	391	79	20.20	1895 . . .	825	190	23.05		
1890 . . .	311	67	21.54	1896 . . .	860	205	23.84		
1891 . . .	303	85	28.05	1897 . . .	881	214	24.29		
1892 . . .	311	79	25.40	1898 . . .	612	109	17.81		
1893 . . .	357	103	30.25	1899 . . .	781	192	24.58		
1894 . . .	732	205	28.01	1900 . . .	823	238	28.92		
				1901 . . .	919	275	29.92		
				1902 . . .	1112	271	24.37		
				1903 . . .	1281	356	27.79		
Total . . .	2405	623	25.9	Total . . .	8094	2050	25.82		

The following table relates to the cases of diphtheria treated in the Municipal Hospital of Philadelphia from 1890 to 1903, inclusive:

Preantitoxin Period.						Antitoxin Period.					
Year.	Cases.	Deaths.	Mortality per cent.	Year.	Cases.	Deaths.	Mortality per cent.	Year.	Cases.	Deaths.	Mortality per cent.
1890 . . .	12	3	25.00	1895 . . .	706 ¹	190	26.91	1895 . . .	706 ¹	190	26.91
1891 . . .	29	1	3.44	1896 . . .	869	193	22.2	1896 . . .	869	193	22.2
1892 . . .	183	48	26.22	1897 . . .	1295	300	23.16	1897 . . .	1295	300	23.16
1893 . . .	217	62	28.57	1898 . . .	1229	297	24.16	1898 . . .	1229	297	24.16
1894 . . .	465	154	33.12	1899 . . .	1373	275	20.02	1899 . . .	1373	275	20.02
				1900 . . .	1299	264	20.31	1900 . . .	1299	264	20.31
				1901 . . .	889	174	19.57	1901 . . .	889	174	19.57
				1902 . . .	601	137	22.79	1902 . . .	601	137	22.79
				1903 . . .	746	170	22.78	1903 . . .	746	170	22.78
Total . . .	906	268	29.58	Total . . .	9007	2000	22.2	Total . . .	9007	2000	22.2

This table shows a mortality reduction in favor of the antitoxin period of 7.38 per cent.

There is no dearth of evidence to prove that the early administration of antitoxin is important if its real advantages are to be gained. Dr. MacCombie's² results at the Brook Hospital, London, show this in a very convincing manner. During the past seven years (1897 to 1903 inclusive) the total number of cases of diphtheria treated in that hospital with antitoxin has been 4812 without a single death occurring among those injected on the first day of the disease. The following table shows these cases arranged according to the day of disease on which the serum was injected, showing the mortality per cent. each year:

¹ Only about one-half of these cases received antitoxin.
² Metropolitan Asylums Board's Annual Report for 1903.

	1897.	1898.	1899.	1900.	1901.	1902.	1903.
Cases (187), first day, mortality was . . .	8.0	0.0	0.0	0.0	0.0	0.0	0.0
Cases (1185), second day mortality was . . .	5.4	5.0	3.8	3.6	4.1	4.6	4.1
Cases (1238), third day, mortality was . . .	11.3	14.3	12.2	6.7	11.9	10.3	17.8
Cases (963), fourth day, mortality was . . .	19.0	18.1	20.0	14.9	12.4	19.8	16.87
Cases (1260), fifth day and after, mortality was . . .	21.0	22.5	20.4	21.2	16.6	19.4	17.1

The *Bulletin* issued by the Health Department of Chicago, February 13, 1904, contains a record of 7435 cases of diphtheria arranged according to day of disease on which antitoxin was administered, showing the mortality per cent. This data appears in the following table:

Day of disease on which antitoxin was injected.	Cases.	Deaths.	Mortality per ct.
First day	586	2	0.34
Second day	1913	28	1.46
Third day	2824	85	3.04
Fourth day	1374	148	10.8
Later than fourth day	986	216	23.1
Total	7433	479	6.44

Among these 7435 cases there were included 608 intubated laryngeal cases, of which 100 died—a death rate of only 16.44 per cent.

It is also stated in the report of the Commissioner of Health of Chicago that there were 7051 exposed persons who were immunized with 500 units each; of these 46 were subsequently attacked, but all recovered.¹

Park² presents the following table showing the mortality of diphtheria treated with antitoxin, including 10,425 cases, arranged according to day of disease on which treatment was commenced:

Day of disease on which antitoxin was injected.	Cases.	Deaths.	Mortality per ct.
First and second day	4,232	267	6.3
Third and fourth day	3,870	656	17.2
After fourth day	1,984	605	30.6
Day unknown	339	44	13.0
Total	10,425	1672	16.0

(Cases moribund or dying within twenty-four hours included.)

Billings³ presents the following tabulation of cases of diphtheria in which antitoxin was administered (1) by Inspectors of the Department of Health, from March 1, 1902, to January 1, 1903, and (2) by physicians (not inspectors), from October 1, 1895, to January 1, 1903:

¹ American Medicine, February 27, 1904.

² Loomis-Thompson, American System of Practical Medicine.

³ New York Medical Journal and Philadelphia Medical Journal, December 12, 1903.

(1) Day of disease on which antitoxin was injected.	Cases.	Deaths.	Mortality per ct.
First day :			
Total cases	125	2	1.66
No moribund cases.			
Second day :			
Total cases	340	15	4.41
Five moribund cases deducted . . .	335	10	2.98
Third day :			
Total cases	320	22	6.87
Six moribund cases deducted . . .	314	16	5.09
Fourth day :			
Total cases	136	19	13.97
Nine moribund cases deducted . . .	127	10	7.87
Fifth day :			
Total cases	65	10	15.38
Four moribund cases deducted . . .	61	6	9.83
Later than fifth day :			
Total cases	71	11	15.49
Five moribund cases deducted . . .	66	6	9.09
Unknown :			
Total cases	10	1	10.0
No moribund cases.			
Total cases	1062	80	7.53
Twenty-nine moribund cases deducted	1033	51	4.93
(2) Day of disease on which antitoxin was injected.	Cases.	Deaths.	Mortality per ct.
First day :			
Total cases	995	62	6.2
Thirty-five moribund cases deducted .	960	27	2.9
Second day :			
Total cases	2526	179	7.0
Seventy-four moribund cases deducted	2452	105	2.6
Third day :			
Total cases	1335	150	11.2
Fifty moribund cases deducted . . .	1285	100	7.8
Fourth day :			
Total cases	485	107	22.0
Forty moribund cases deducted . . .	445	67	15.0
Fifth day and over :			
Total cases	425	121	26.0
Sixty-two moribund cases deducted .	363	59	16.0
Unknown :			
Total cases	440	54	12.2
Twenty-one moribund cases deducted	419	33	7.8
Total cases	6206	673	10.84
232 moribund cases deducted . . .	5924	391	6.6

At the Willard Parker Hospital (New York), during the first nine months of 1895, the results were as follows:¹

Day upon which the serum treatment was begun.	Cases.	Mortality per cent.
First day	108	10.09
Second day	130	25.19
Third day	116	34.19

From 1895 to 1903 inclusive, 7469 cases of diphtheria were injected with antitoxin in the Municipal Hospital, Philadelphia. The following table shows these cases arranged according to day of disease on which the antitoxin was administered, showing deaths and mortality per cent.:

¹ Winters, Medical Record, June 20, 1896.

Day of disease on which antitoxin was injected.	Cases.	Deaths.	Mortality per cent.
First day	969	99	10.31
Second day	2325	268	15.82
Third day	1761	415	23.56
Fourth day	1109	350	31.46
Later than fourth day	1815	439	23.24
Total	7469	1671	22.37

From 1894 to 1900 inclusive, there were 1830 cases of diphtheria admitted to the Municipal Hospital, Philadelphia, which did not receive antitoxin. In the following table these cases are arranged according to day of disease on which admission to the hospital occurred:

Day of diseases on which cases were admitted to hospital.	Cases	Deaths.	Mortality per cent.
First day	186	20	10.75
Second day	411	66	16.06
Third day	373	81	21.71
Fourth day	415	146	34.94
Later than fourth day	445	137	30.78
Total	1830	449	24.53

In taking a comparative view of the last two tables the showing in favor of the antitoxin treatment is not very marked. It should be understood that in neither of these series of cases was any effort made to eliminate those admitted moribund, or believed to be hopeless, or even those in which the diphtheria followed in the wake of some other affection, like measles or scarlet fever. The history in each case as to the day of the disease on admission was obtained either from the parents of the patient or from the patient himself when old enough. It is not improbable that this information was often inaccurate. But histories as to duration of illness are, of necessity, almost always obtained in this way.

We must confess to a feeling of disappointment in the results obtained from the use of antitoxin in the Municipal Hospital. We had fervently hoped that this agent would effect a striking reduction in the mortality among our patients, but the statistics of the hospital do not indicate any great saving of life. The reduction in the death rate from diphtheria in the hospital has at the most been about 7 per cent. It may be that many of our patients are received at too late a period of the disease to respond to the serum treatment. It may also be possible that in our early experience with antitoxin the serum may not have been employed in sufficiently large doses, although the amount given was that generally advocated at the time. Park's remarks on dosage in animals (extract from *Pediatric Section, New York Academy of Medicine, November 10, 1904*; published in *Archives of Pediatrics*, December, 1904) may likewise apply to the human subject. Park states that a given amount of diphtheria antitoxin injected into an animal immediately after a fatal amount of the toxin will save the life of the animal. If a delay of four hours occurs before the injection of the antitoxin, then ten times the amount of the latter is necessary in

order to protect the animal. If six or eight hours' delay occurs, one hundred times the amount of antitoxin becomes necessary. Park adds that the longer one waits before giving the antitoxin the greater is the chance for the toxin to combine and enter into some definite relation with the cells.

The Paralysis Incidence.—It is not claimed that the paralysis incidence in diphtheria has been lessened by antitoxin. On the contrary, it is believed by many that this sequela is more frequently seen now than formerly. Baginsky says that "paralysis is more frequent under antitoxin than before; perhaps because more children remain alive."

In 1000 cases of diphtheria carefully observed by Lennox Browne he found that paralysis was more common than in previous years when antitoxin was not employed.

Goodall,¹ of London, has shown that paralysis became more frequent in the Metropolitan Asylums' Board hospitals after the introduction of antitoxin. He presents the following table showing the percentage incidence of paralysis in the Board's hospitals from 1893 to 1897, inclusive:

	Non-antitoxin.		Antitoxin.		
	1893.	1894.	1895.	1896.	1897.
Eastern Hospital	12.1	10.8	16.0	21.4	15.1
Northwestern Hospital	14.0	11.1	18.9	14.1	12.8
Western Hospital	18.1	8.2	17.7	21.5	11.0
Southwestern Hospital	14.3	18.3	22.0	20.6	20.5
Southeastern Hospital	16.2	20.2	34.7	42.3	45.9
Total	14.3	13.2	20.1	21.3	20.3

Alleged Ill Effects of Antitoxin.—In the vast majority of cases no immediate ill effects are noticeable. An abscess at the site of the injection may occur, but this is preventable.

Many observers believe that antitoxin has increased the incidence of nephritis. It does seem that albuminuria is more frequently seen now than formerly. Referring to the results in his 1000 cases of diphtheria, Lennox Browne says his figures show a very considerable and undoubted increase in the proportion of cases of nephritis under serum treatment as compared with the old. Speaking of Baginsky's experience to the contrary, he remarks: "It is only fair to quote the experience of Professor Baginsky. . . . On a comparison of 993 cases without serum and 525 with serum, he has come to the conclusion that the injection of serum does not increase the frequency of nephritis, giving tables in support of his contention. This observer is careful to give separate and widely different figures for clinical nephritis, as distinguished from that observed *post-mortem*."

Hansemann, Washbourn, Goodall, and Lennox Browne have noted the liability to anuria under serum treatment. The last-named writer says he was particularly unfortunate in his own early experience in this respect, as 6 out of a series of 8 patients died with anuria as the most prominent symptom.

R. W. Marsden,² of London, believes that the early use of antitoxin

¹ British Medical Journal, 1899, p. 197.

² Ibid., 1900, vol. II, p. 658.

lessens the liability to albuminuria, and that when it appears late in diphtheria it may be due to antitoxin. He says that "though it may have an irritant effect upon the kidneys, yet this is by no means the rule, and in any case its action is only temporary."

Winters,¹ of New York, one of the attending physicians to the Willard Parker Hospital, believes that pneumonia in diphtheria has become more frequent since the employment of the serum treatment. He says that "the pneumonia of the antitoxin cases of diphtheria differed from the pneumonia we were in the habit of seeing in diphtheria; that it was a totally different disease from that seen before in the course of diphtheria; that it occurred as a sequela and not as a complication." He regards it as septic in character.

In an earlier part of this article we called attention to the frequency of bronchopneumonia in the laryngeal form of diphtheria, and expressed the belief that it resulted from diphtheritic involvement of the respiratory tract. It is true that bronchopneumonia often occurs late in the disease, and even at times during convalescence from the faucial form of diphtheria, but we have never felt that it was due to the serum treatment.

Before concluding it may be well to mention the fact that more than one death has been reported as immediately following the injection of the serum. This accident has been almost entirely confined to the use of the serum for immunizing purposes. While no very satisfactory explanation has been given for the occurrence of these sudden deaths, it is not believed that they were caused by the serum *per se*.

The only ill effect which we are able to attribute to antitoxin with any degree of certainty is a peculiar exanthem, often attended with rise of temperature and more or less joint pains.

Antitoxin Eruptions. FREQUENCY.—The use of antitoxic serum in diphtheria is followed, in a certain proportion of cases, by a train of phenomena, the most conspicuous of which is the development of a cutaneous eruption. The proportion of cases in which antitoxin rashes develop is most variable. Hartung has collected from the literature a series of 2661 injections, of which 294, or 11.4 per cent., developed rashes. 253 of these eruptions are accounted for in the following table

	Eruptions.	Injections.	Per cent.
Heubner (Berlin cases)	54	298	18.1
Heubner	22	77	28.5
Boginsky	49	525	9.3
Soltmann	5	89	5.6
v. Ranke	5	118	4.2
Seltz	20	140	14.3
	4	180	2.22
Forster	7	73	9.6
Schucolty	4	38	10.5
Gunther	3	33	9.0
Bokai	11	120	9.1
	30	147	20.4
Moizard, Paris	33	231	14.2
Risel, Halle	6	114	5.2
	253	2233	11.08

¹ Medical Record, June 20, 1896.

The Imperial Board of Health of Germany reports 4358 cases of diphtheria injected with serum from January to July, 1895, with the production of 354 rashes, or 8.1 per cent.

Among 78 cases of diphtheria treated in the Scarlet Fever and Diphtheria Hospital of New York, in 1901, rashes occurred in 25.4 per cent.

The Investigating Committee of the Clinical Society of London collected records of 663 cases; 220 of these, or 33.1 per cent., developed antitoxin rashes.

Lennox Browne¹ noted 38 eruptions in 100 cases. Berg² gives the following figures for the Willard Parker Hospital of New York for four months:

	Cases.	Rash.	Per cent.
May	107	18	17
June	103	23	23
July	62	19	33
August	65	22	33
Total.	337	82	24

The great variability in the frequency with which antitoxin eruptions develop may be best appreciated when it is stated that Monti, of Vienna, observed rashes in 52 per cent. of one of his series of cases, whereas Hager did not observe a rash in a single instance among 61 cases.

In our own experience an eruption has developed in about 20 per cent. of the cases injected.

DATE OF APPEARANCE OF ERUPTION.—The rash may appear in from one day to one month after the injection of the serum. The subjoined table will show the day of occurrence of 120 antitoxin eruptions observed by us in the Municipal Hospital of Philadelphia. It will be seen that the greatest number of rashes occurred upon the sixth, seventh, and eighth days after the administration of the serum. Indeed, by actual computation over 49 per cent. of the total number appeared on these days.

The date of appearance of the rash depends much upon the particular serum employed. A few years ago we used a serum the rashes from which quite uniformly appeared about the end of fourteen days.

DAYS UPON WHICH ANTITOXIN ERUPTIONS DEVELOPED IN 120 OF OUR CASES.

Rash appeared in 1 case on the second				day after the serum injection.		
"	"	6 cases	"	fourth	"	"
"	"	6 "	"	fifth	"	"
"	"	18 "	"	sixth	"	"
"	"	17 "	"	seventh	"	"
"	"	24 "	"	eighth	"	"
"	"	5 "	"	ninth	"	"
"	"	7 "	"	tenth	"	"
"	"	5 "	"	eleventh	"	"
"	"	7 "	"	twelfth	"	"
"	"	5 "	"	thirteenth	"	"
"	"	5 "	"	fourteenth	"	"
"	"	1 case	"	fifteenth	"	"
"	"	8 cases	"	sixteenth	"	"
"	"	3 "	"	seventeenth	"	"
"	"	1 case	"	eighteenth	"	"
"	"	1 "	"	twentieth	"	"

¹ Diphtheria and its Associates, London, 1895.

² New York Medical Record, 1898, pp. 865-873.

In the report of the Clinical Society of London, the largest number of rashes appeared from the seventh to the twelfth day; the figures are as follows:

DAY OF APPEARANCE OF ANTITOXIN ERUPTIONS.

First to sixth day	25 cases
Seventh to twelfth day	147 "
Thirteenth to eighteenth day	34 "
Nineteenth to thirty-first day	6 "

The rashes noted by Lennox Browne appeared for the greater part from the seventh to the twelfth day. The statement is made by some writers that the scarlatinoid rashes are prone to occur early, in the neighborhood of the third day. We have seen some rashes of this character occur quite early.

CHARACTER OF THE ERUPTION.—In our experience the vast majority of the rashes have been of an urticarial character, either made up of frank wheals or consisting of an urticarial erythema. Next in frequency have been the rashes belonging to the class of polymorphous erythema.

These may consist of irregular marginated and non-elevated patches of redness, or may show a distinct tendency to annular or gyrate configuration. It is not uncommon to see an erythema made up of small, round, red patches with perfectly pale centres.

In other cases the erythema may be of the *scarlatinoid* type and bear a close resemblance to the exanthem of scarlet fever. These appear to have occurred much more frequently in New York City than in Philadelphia. In other cases the rash may be a *morbilliform erythema*, looking not unlike the eruption of measles.

Vesicular and *bullous* eruptions are quite uncommon; but we have observed one well-pronounced case, which is shown in the accompanying photographs. We have also observed a case in which there was extravasation of blood into the vesicles. *Purpuric* antitoxin eruptions are not very frequent, for of many hundreds of rashes that have occurred in the Municipal Hospital we have seen not more than eight or ten characterized by hemorrhage into the skin.

Antitoxin eruptions are frequently polymorphous, exhibiting wheals, patches of non-elevated erythema, and occasionally papules and vesicles. Mixed urticarial and erythematous lesions are frequently observed.

Indeed, all of the lesions which may occur in erythema multiforme may be present in the rashes following serum injections. Most of the rashes are accompanied by severe itching; this is particularly complained of by adults, who are, perhaps, better able to give expression to their discomfort.

Edema of the skin is commonly noted in association with antitoxin rashes. The face is puffed, particularly about the eyelids, and not infrequently the penis, scrotum, and feet are oedematous.

Among the 220 rashes recorded by the Clinical Society of London, 161 were erythematous, 37 were urticarial, 17 were mixed, and 5 were petechial; 2 of the 5 petechial cases died. Of 33 rashes noted by Moizard,

PLATE LX.



An Unusual Antitoxin Eruption exhibiting Erythematous Patches
on the Trunk and Vesicular Lesions on the Face.



PLATE LXI.



The Same Patient as Plate LX , showing the Vesicular
Character of the Lesions on the Face.



14 were urticarial, 9 scarlatiniform erythema, 9 polymorphous erythema, and 1 purpura.

DISTRIBUTION.—The distribution of the eruption is extremely irregular. It may occur upon any portion of the cutaneous surface. It is noted with particular frequency about the arms, legs, and buttocks, although the trunk is scarcely less commonly attacked. The face often escapes, but by no means always.

The most frequent region for the appearance of the rash is the site of the injection. It is quite common for an erythematous or urticarial eruption to appear about the cutaneous puncture and the surrounding skin within twenty-four hours after the injection; this frequently disappears only to return some days later as the herald of the general eruption. Among the 220 antitoxin rashes recorded by the Clinical Society of London, 46 were first seen at the site of the injection.

The eruption may consist of but a few scattered patches, or it may be so profuse as to involve the greater part of the cutaneous surface.

The eruption ordinarily persists for about forty-eight hours, although in some cases it may last three, four, or five days. The purpuric rashes continue much longer. Occasionally the rash will begin to fade and almost disappear, and then in twenty-four or forty-eight hours reappear.

RECURRENT RASHES.—The eruption following the use of diphtheria antitoxin is occasionally subject to recurrence. The rash may disappear and return in a few days or several weeks afterward. Among 134 rashes observed by us within a year and a half, there were 14 recurrent rashes. The earliest relapse occurred three days after the first eruption and the latest seventeen days. There is sometimes more than one recurrence. The Clinical Society of London reports 11 recurrent rashes among 220 eruptions collected. The following table gives the day of appearance and of recurrence of the cases observed by us:

RECURRENT ANTITOXIN ERUPTIONS.

Primary rash appeared in :										
1 case	7 days after serum injection, and again	3 days later.								
1	"	7	"	"	"	"	"	5	"	"
1	"	4	"	"	"	"	"	17	"	"
1	"	7	"	"	"	"	"	4	"	"
1	"	6	"	"	"	"	"	14	"	"
1	"	10	"	"	"	"	"	4	"	"
1	"	6	"	"	"	"	"	5	"	"
1	"	8	"	"	"	"	"	7	"	"
1	"	8	"	"	"	"	"	7	"	"
1	"	8	"	"	"	"	"	7	"	"
1	"	6	"	"	"	"	"	14	"	"
1	"	10	"	"	"	"	"	4	"	"
1	"	6	"	"	"	"	"	5	"	"
1	"	6	"	"	"	"	"	6	"	"
<hr/>										
Total 14										

Constitutional Symptoms.—Antitoxin rashes are commonly accompanied by constitutional disturbance of a more or less pronounced character. In the majority of cases there is elevation of temperature

with its usual concomitant symptoms. The pyrexia is extremely variable; in some cases there may be hyperpyrexia.

We have occasionally observed temperatures in children of 104° and 105° F. More commonly the fever does not rise above 101° or 102° F. In the 220 rashes reported by the Clinical Society of London, fever accompanied the eruption in 136 of them.

The fever lasts ordinarily from twenty-four to seventy-two hours, although it may persist longer. It declines, as a rule, with the subsidence of the rash. Headache is commonly associated with the fever and a variable amount of prostration is present. In some cases the prostration is quite pronounced.

Vomiting occurs occasionally in children, and now and then there is diarrhœa. Where the temperature is high delirium is said to occur (Sevestre and Martin). We have not observed delirium in any of our cases.

A very common symptom accompanying the antitoxin rash is pain in the joints; adults often bitterly complain of this arthralgia. Articular swelling is noted in a certain proportion of cases. The wrists, elbows, shoulders, knees, and ankles are the joints most commonly attacked. The swelling usually subsides in a few days.

The Clinical Society of London reports arthropathies 40 times among 663 cases of diphtheria; in 35 of these cases the joint symptoms accompanied the antitoxin eruption.

Causation of the Serum Phenomena.—The phenomena which develop in a certain proportion of cases after the administration of antidiphtheritic serum are without doubt dependent upon something which is contained in the injected fluid. There is strong reason to believe that the antitoxic principle itself has little or nothing to do with the eruption and other manifestations produced. It has been quite conclusively proven that plain horse serum when injected into individuals will produce eruptions of the character described in about the same proportion of persons as the diphtheria antitoxic serum.

The serum of non-immunized horses was injected by Bertin into a number of children suffering from diphtheria with the development of rashes in a considerable proportion of them. Four children suffering from an ordinary sore throat were injected by Sevestre with serum of non-immunized horses, with the production of an erythema in each one.

Johannsen,¹ of Christiania, administered hypodermically 2 to 15 c.c. of pure blood serum from a healthy non-immunized horse to 23 persons free of diphtheria. The serum given to 19 of the individuals was filtered; 4 received unfiltered serum. A more or less generalized erythema developed in 12 of the 23 patients in from one to eleven days. The filtered serum produced less disturbance than the unfiltered.

It has long been known that the injection into an animal of an alien or heterogeneous blood serum—*i. e.*, a serum derived from an animal of another species—is followed by toxic symptoms.

¹ Johannsen, Bertin, and Sevestre. Cited by Berg, *loc. cit.*

Rumno¹ believes that the toxic effect of blood serum depends upon the action of special toxalbumins. Alexander Schmid² is of the opinion that the toxic effect is due to the action of the soluble fibrin ferment of one blood serum upon the second animal.

If Ehrlich's side-chain theory stands the test of time it will probably be found that the serum injected contains a substance which acts as an intermediary body.

Berg, after using antitoxic serum filtered through a Chamberland filter, and comparing the results with unfiltered serum, concluded that filtered antitoxin is less likely to give rise to rashes. Park, of New York, is not convinced that this is actually so.

The wide variability in the production of serum rashes is doubtless due to two factors: 1. Individual susceptibility or predisposition, and, 2, peculiarities in the blood serum of certain horses. There can be no question that the serum of some horses gives rise to a larger percentage of antitoxin rashes than that of others.

Where the serum of an animal produces an unusually large number of eruptions, that animal had better be given up as a source of antitoxin.

Diagnosis of Serum Rashes.—It is often a matter of difficulty to distinguish between an antitoxin eruption and the eruption of measles or scarlet fever, more particularly the latter. Secondary infection with scarlet-fever poison during the course of diphtheria is not an uncommon occurrence. When a scarlatiniform rash develops in a patient who has been given antidiphtheritic serum, the question arises, Is the rash the result of the serum, or is it an expression of scarlet fever?

No more difficult problem in differential diagnosis arises than in these cases. The diagnosis may be easy when the scarlet-fever symptoms are complete and well marked. When there is vomiting, rapid rise of temperature, an aggravation of the existing angina, a characteristic tongue, and an intense, diffuse, punctated rash, the nature of the phenomena may be readily divined. But when, as so often happens, there is moderate pyrexia (100° or 101° F.), and a diffuse rash of moderate intensity, the solution of the diagnostic problem is at times impossible. The difficulties are increased by reason of the fact that diphtheria patients suffer from an angina and from glandular enlargement, and the antitoxic serum may produce fever, a scarlatinoid rash, vomiting, and prostration.

In our experience at the Municipal Hospital, scarlatinoid eruptions have formed but a very small percentage of the serum rashes. We have observed from time to time a large number of scarlatinoid rashes accompanied by more or less fever in the diphtheria wards, but we have regarded such cases as scarlet fever and have sent them to the "mixed ward" where cases of double infection with diphtheria and scarlet fever are treated. Although these wards always contain some well-pronounced cases of scarlet fever, the patients sent from the diph-

¹ Quoted by Berg, loc. cit.

² Ibid.

DIPHTHERIA

wards with the scarlatinal rashes have rarely contracted scarlet

This experience has seemed to us to afford confirmatory, though not conclusive, evidence that the diagnosis was correct.

The city of New York scarlatiniform rashes after the injection of toxic serum seem to have been more common than in Philadelphia, and within recent months, during which time there has been no epidemic of diphtheria at the Philadelphia Municipal Hospital, the New York Board of Health serum, it has appeared to us that scarlatinoid rashes from the serum have been more frequent.

The features which tend to indicate that the rash is of serum origin and not the exanthem of scarlet fever are: its development at about the same time after the injection, the moderate grade of the accompanying fever, the presence of severe itching, the absence of a recurrent fever, and the scarlatinal tongue, the occurrence of joint pains or pains in the muscles, irregularity in the development or distribution of the rash, the brevity of its duration, and the absence of consecutive desquamation.

It must be remembered, however, that all of these phenomena have but a relative value in the diagnosis and that in many cases, after due consideration of all the symptoms, the diagnosis remains obscure. Other observers of experience have recognized similar difficulties in diagnosis.

CHAPTER XV.

DISINFECTION.

Disinfection of Rooms.—The best method of room disinfection known to us at the present time is the use of formaldehyde gas or sulphur dioxide. It must be remembered, however, that these gaseous substances accomplish largely a surface disinfection and cannot be depended upon to penetrate to any considerable degree such articles as mattresses, upholstered furniture, etc.

In view of certain disadvantages of sulphur fumigation, to which reference will be made later, formaldehyde gas is recognized at the present day as the most useful and suitable gaseous disinfectant.

The advantages of *formaldehyde* are due to its active germicidal properties, to its non-toxic effects upon the higher forms of animal life, and to the fact that it does not injuriously affect fabrics, metals, etc. It appears to exert no detrimental influence whatever upon silks, woollens, cotton, linen, tapestries, carpets, or oil paintings. It is the only efficient disinfectant that can be employed in a furnished apartment without any destructive influence upon the contained objects.

The *germicidal value* of formaldehyde is doubtless due to its property of combining with the nitrogenous organic matter with which it comes in contact. It destroys bacteria by uniting with the albuminoids which make up the protoplasm of these micro-organisms. It likewise acts as a *deodorant* by combining with the nitrogenous products of decaying animal matter and forming new chemical compounds.

Formaldehyde in concentrated volume rapidly kills the ordinary bacteria; if the amount of gas be sufficient and the exposure prolonged, most all of the disease-producing spores are also destroyed.

Despite its strong germicidal action, formaldehyde is not poisonous to the higher forms of life. Roaches, bed-bugs, vermin, and such animals as rats, guinea-pigs, and rabbits are not killed by moderately long exposures. An intense irritation of the mucous membranes is, however, produced, which may terminate fatally.

Mosquitoes directly exposed to a concentrated volume of the gas will succumb, but formaldehyde is inferior to sulphur fumigation for the destruction of these insects.

Formaldehyde is sold in commerce in 40 per cent. solution under the name of formalin. In cold weather a deterioration in the strength may occur as a result of the precipitation of some of the insoluble allied products.

PREPARATION OF THE ROOM FOR DISINFECTION.—Inasmuch as the gas is readily lost by leakage it is necessary to seal all the cracks and

crevices through which an escape might take place. Windows should be tightly closed, and all crevices about them and around the doors sealed with cotton-batting, or, better, with strips of gummed paper. Keyholes should be plugged and registers and flues tightly closed. An open fireplace must be carefully sealed. After the room is made as air-tight as possible the various infected objects are to be spread out so that their surfaces are fully exposed to the gas. Wash-lines may be strung across the room, upon which should be suspended bed-linen, clothing, towels, etc. Closets, bureau-drawers, and all similarly enclosed spaces should be opened so as to be freely permeated by the disinfectant.

The amount of gas to be employed and the duration of the exposure will depend, to a certain extent, upon the method used.

Rooms are ordinarily disinfected by formaldehyde by one of several methods. The gas may be generated from its watery solution by *distilling it in a retort*. Formalin is used for this purpose; it is advised that 1 per cent. of glycerin be added to raise the boiling point and lessen the polymerization of the formaldehyde.

Ten ounces of formalin should be used for every 1000 cubic feet of air space.

The room should be kept closed for at least six hours and preferably longer.

Another method which is much employed is the production of the gas from a *formaldehyde generator or lamp* by the dehydrogenation of methyl or wood alcohol, mixed with water, over incandescent platinum in a finely divided state on asbestos disks.

The chief advantage claimed for this method lies in the fact that nascent formaldehyde is liberated and that the gas is more active in this state. There is less conversion of the gas to paraform and a less persistent clinging of the odor in the room.

Spraying is a very convenient method of disinfection, but must be employed with thoroughness in order to be efficient.

The plan at present employed by the Philadelphia Board of Health is to spray all surfaces of the room to be disinfected with a mixture of equal parts of water and a saturated solution of formaldehyde gas in water (formalin). Three pints of this mixture are used for each 1000 cubic feet of air space in the room. From special laboratory investigations carried out by the Board of Health, better results were obtained from the employment of strong solutions of formaldehyde in the form of a fine spray than from any other method. By this means 100 per cent. of the test objects placed in the room were killed.

It was also found that formaldehyde, applied in this manner to bedding, had much more penetrating power than when applied as a gas.

"Of 900 beds, including mattresses, covers, and pillows of different qualities, that were thoroughly sprayed on all surfaces in this manner, all were completely disinfected, as demonstrated by the death of test objects placed in different parts of the bedding. This result has led

to the abandonment in most cases of the former practice of removing bedding from the sick-room for disinfection by steam."¹

The formalin (50 per cent. dilution) is rapidly sprayed over the walls, floors, and ceiling under pressure of compressed air. A long elbow gas-pipe is used to reach the ceilings and upper portions of the walls.

The method employed by the Chicago Board of Health is as follows: Sheets are strung diagonally across the room upon wash-lines. Formalin is then sprayed upon the sheets by a specially devised sprinkler. The spraying must be done quickly on account of the irritating properties of the gas, and yet care must be used to apply the formalin in small drops and not in large splashes, so as to secure the maximum surface for evaporation and the freest evolution of the gas.

For each 1000 cubic feet of air space no less than *ten ounces of formalin* should be used. It is advisable for the disinfecter to wear rubber gloves to protect the hands from the spray.

The room is kept tightly sealed for twenty-four hours, after which it is thoroughly aired and sunned.

In the use of any of the formaldehyde fumigation methods it is highly advantageous to use *spraying* as a *supplementary* measure. The formalin in half-strength may be sprayed upon the floors, in the closets and corners, and upon bedding, furniture, etc.

Another method of formaldehyde disinfection is by *heating paraform*, which is one of the polymeric forms of formaldehyde. This is a white powder which may be compressed into tablets or pastils. These are heated in small lamps and the gas driven off. This method is useful in the disinfection of small, tightly sealed places of less than 1000 cubic feet, such as closets.

For each 1000 cubic feet no less than two ounces of paraform should be used.

Sulphur Dioxide.—The gas evolved by burning sulphur is an excellent surface disinfectant, but has certain serious disadvantages. Its injurious influence upon cottons and linen fabrics, and especially upon the coloring matter in various articles, unfits it for use in furnished apartments.

Sulphur dioxide has a destructive effect not only upon bacteria, but also upon animal life. It may, therefore, be advantageously employed whenever it is desired to kill rats, roaches, fleas, mosquitoes, vermin, etc. It may also be used in unfurnished apartments when formaldehyde is not available. It has the further advantage of being cheap and readily procurable.

For a room of 1000 cubic feet of air space, five pounds of sulphur should be burned. A considerable amount of moisture must be present to convert the sulphur dioxide into sulphurous acid. The method usually employed is as follows:

The room is prepared as for formaldehyde fumigation. The sulphur, in the form of flowers of sulphur, is placed in an iron pot or pan and

¹ From the Bulletin of the Bureau of Health, Philadelphia, December 3, 1904.

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in a tub of water. The water surrounding the pot lessens of fire and at the same time furnishes the necessary moisture. It may be ignited by means of hot coals or by lighting alcohol poured into a concavity in the sulphur.

When a number of sulphur pots had better be used. If life the fumigation should continue for two hours; destruction of micro-organisms requires an exposure of from two to four hours.

Disinfection of Various Articles. BEDDING.—The gaseous disinfectants cannot be relied upon to disinfect mattresses that are deeply soiled. These should be subjected to steam under pressure. Most cities have established steam disinfecting plants for this purpose. If the facilities are not present for thorough disinfection of mattresses like these articles had better be destroyed by fire.

Upholsteries and other wooden and metallic furniture may be washed with a 5 per cent. solution of carbolic acid or the same strength of formalin.

CARPETS AND RUGS.—Carpets and rugs should be exposed to the gaseous disinfectants and in addition thoroughly sprayed with a 5 per cent. solution of formalin. Where the carpet or rug has been deeply soiled by infectious discharges it is best to have the same subjected to steam disinfection after the fumigation of the room is performed.

BOOKS.—Unbound books should be subjected to steam disinfection. Bound books may be thoroughly disinfected in a specially devised, small, air-tight formaldehyde chamber in which a partial vacuum may be produced. In households where no special apparatus is at hand a few drops of formalin should be discreetly sprinkled upon every page of the book. The volume with its pages open should then be placed in an air-tight box, chest, or drawer, and an excess of formalin placed therein. The exposure should continue for not less than twenty-four hours and the room should be kept warm.

LETTERS AND MONEY.—Letters may be readily disinfected by clipping away a corner of the envelope, dropping in with an eye-pipette a few drops of formalin, and placing the same with an excess of formalin in a tight box for six hours in a warm room. Dry heat or steam are surer disinfectants, but often are not available. Paper money may be sprayed with formalin and then subjected to the same treatment as letters. Metal money can be boiled, or cleansed in a 5 per cent. carbolic acid solution.

CADAVERS.—The bodies of patients who have succumbed to infectious diseases should be thoroughly enveloped in a sheet immersed in a 5 per cent. solution of carbolic acid, or a 1:1000 solution of corrosive sublimate. The sheet is nicely adjusted to the body and held together by pins.

The best disposition of such cadavers is by cremation. Where this cannot be carried out, the body should be surrounded with twice its weight of freshly burned lime in a tight coffin and interred at least six feet beneath the soil.

Embalming with strong solutions of formalin or arsenic destroys all but the surface infection, and this may be treated with solutions of carbolic acid, corrosive sublimate, or formalin.

VEHICLES.—Ambulances, carriages, street cars, and the like, are best disinfected by running them into a tightly closed compartment which may be quickly filled with large quantities of strong formaldehyde gas. In a specially built structure of this kind satisfactory disinfection may be effected in an hour. Vehicles which can be tightly closed may be thoroughly sprayed with a 5 to 10 per cent. solution of formalin and the vapor allowed to act for about six hours.¹

¹ In preparing the above article the writers have consulted the excellent book on "Disinfection and Disinfectants," by Dr. M. J. Rosenau, Director of the Hygienic Laboratory and Passed Assistant Surgeon U. S. Public Health and Marine Hospital Service.



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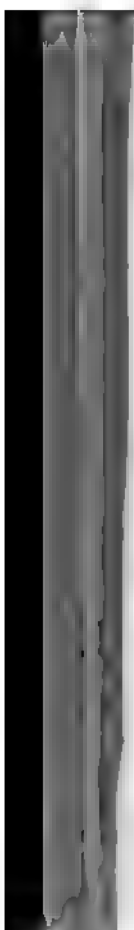
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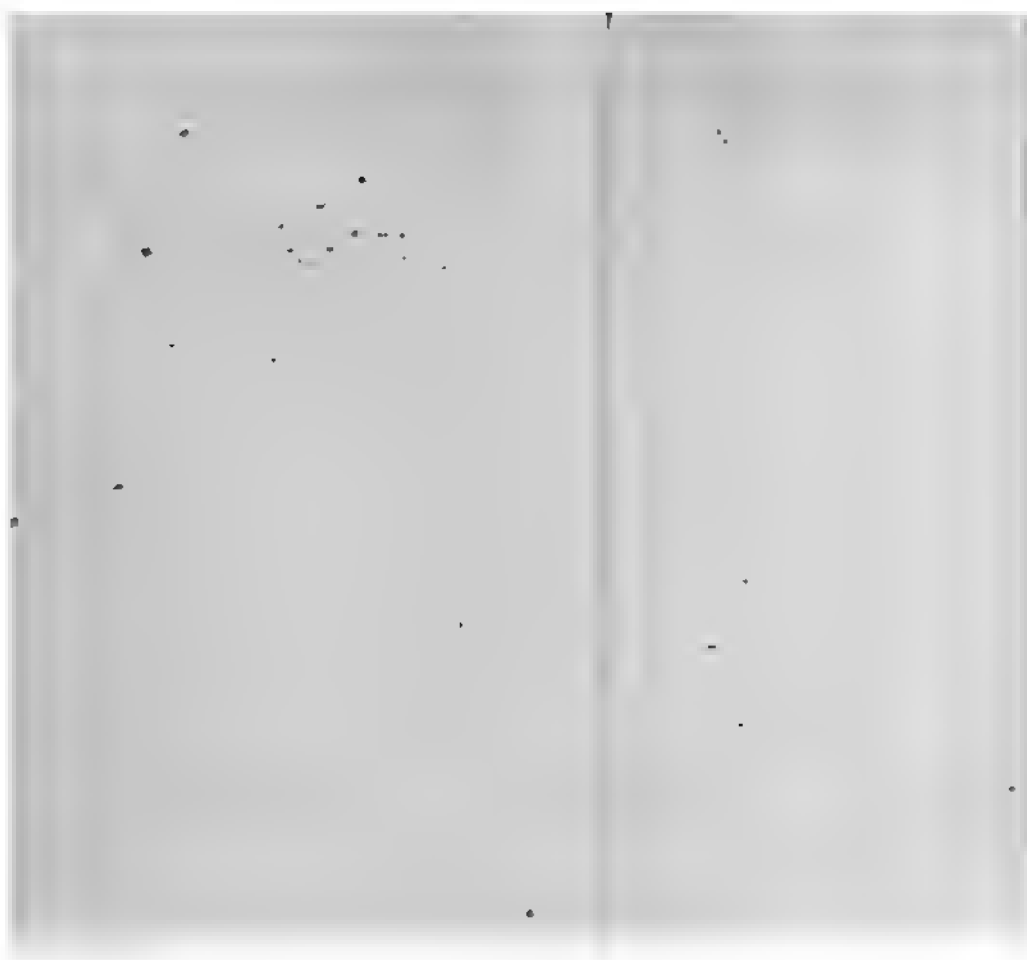
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